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EXPERIMENTAL STUDIES IN ECZEMA *

I. STUDY OF THE SENSIBILITY OF THE SKIN OF RABBITS TO CHEMICAL IRRITANTS UNDER EXPERIMENTALLY INDUCED CONDITIONS

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The theories as to the cause of eczema are well known and need not here be reviewed. From clinical observations, it appears that the skin of patients with eczema is in an increased state of sensibility. Weidenfeld,[1] Schultz,[2] Hammer,[3] Bloch [4] and others have shown that the uninvolved skin of the majority of patients with eczema reacts to externally applied irritants in a much greater percentage than normal persons.

Few experimental studies, with the exception of those of Luithlen, have been reported in the direction of determining the pathogenesis of an increased sensibility of the skin as well as conditions that decrease such sensibility.

In this work, Luithlen [5] employed cats and rabbits. Varying dilutions of croton oil were painted on the shaven skin of these animals the resulting reactions being compared to those following similar applications to another skin area of the same animal subsequent to experiments relative to diet, the injection of calcium chlorid, sodium oxalate and hydrochloric acid. He observed that the skin of rabbits fed on an

* From the Research Institute of Cutaneous Medicine, Philadelphia. Read at the Forty-Seventh Annual Meeting of the American Dermatological Association, Minneapolis, June, 1924.

1. Weidenfeld, S.: Beitrage zur Pathogenese des Ekzems, Arch. f. Dermat. u. Syph. **111**:891-984, 1912.

2. Schultz, J. H.: Die Prüfung der Hautreaktion auf chemische Reize, Jahrb. f. Kinderh. **78**:347-349, 1913.

3. Hammer, F.: Ueber Hautreize und deren Verwendung, Dermat. Wchnschr. **75**:969-982, 1922; ibid., 996-1006.

4. Bloch, B.: Eczema and Diathesis, Ztschr. f. klin. med. **99**:2-14, 1923

5. Luithlen, F.: Tierversuche über Hautreaktion, Wien. klin. Wchnschr. **24**:703-705, 1911.

exclusive diet of oats acquired a greater sensitiveness to croton oil than that of those fed exclusively on green fodder and that the administration of hydrochloric acid or sodium oxalate increased this reaction, while the administration of calcium salts diminished it. In a subsequent paper Luithlen [6] studied the mineral metabolism of rabbits on an all oat diet and on a diet of all greens, and after the administration of hydrochloric and oxalic acids, by determining the amount of bases ingested and excreted.

From his results, Luithlen concluded that feeding oats exclusively produces in the animal a negative calcium balance. On an all green diet, ample retention of all bases takes place.

From a comparison of the experimental and clinical results of these investigations, Luithlen concludes that the sensitiveness of the skin in rabbits—its reaction to externally applied chemical irritation—is dependent on processes within the organism in the metabolism of mineral salts, and the amount and proportion of the single cations, calcium, magnesium, potassium and sodium; and that the reaction of the skin can be influenced by feeding and introducing various substances into the organism.

To determine whether the processes that lead to a change in skin reaction take place in the skin itself or in its chemism, Luithlen [7] determined the content of rabbit skin in calcium, magnesium, potassium and sodium while feeding the animal with oats as well as greens, and after injecting hydrochloric acid and sodium oxalate. This study showed that variations in the content of bases in the skin occur after changing the food as well as after the injection of hydrochloric acid or sodium oxalate.

Luithlen states that the total content of the skin in calcium, magnesium, potassium and sodium, as well as the proportion of these cations to one another, conforms with the results of his aforementioned investigations. He further states that minor changes, which would not affect the total content of the bases, are likely to change the functions of the organism, as well as the processes of the skin and its reaction to external inflammatory injury, by altering the relation of the single bases to one another. He states that his research in metabolism explains the influence of the changed feeding on the entire metabolism, and shows that changes and disorders of the latter, like uric acid diathesis, gout, diabetes, autointoxication and other processes may initiate far-

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6. Luithlen, F.: Das Gegenseitige Kationenverhältnis bei verschiedener Ernährung und bei Säure-Giftung, Arch. f. exper. Path. u. Pharmakol. **68**:219-230, 1912.

7. Luithlen, F.: Veränderungen des chemismus der Haut bei verschiedener Ernährung und Vergiftungen, Arch. f. exper. Path. u. Pharmakol. **69**:365-374, 1912.

reaching changes in mineral metabolism. He concludes that these chemical investigations of the skin demonstrate that together with a change in metabolism there is also a change in the chemistry of the skin, which results in its altered reaction, and that this may now be utilized to explain the etiology of eczema.

PURPOSE OF THE STUDY

The purpose of the study was to repeat the experimentation of Luithlen concerning the influence of diet. Our object was to determine the effect of the administration of acids and other substances which Luithlen observed modified the sensibility of the skin of rabbits and cats to externally applied irritants; to supplement Luithlen's experiments with further dietary studies and experiments to determine the rôle that certain organs possibly play in altering sensibility of the skin, by removing or injuring these organs and to correlate these experiments with blood chemistry studies.

METHOD EMPLOYED

Adult healthy rabbits, of both sexes, of variable color and weight, were employed in most of the experiments. In a few instances, cats were employed.[8]

Prior to experimentation, the animal was fed on a mixed diet. With rabbits, this consisted of oats mixed with beet pulp, hay, greens and bread. One or the other or a combination of these foods was alternately fed. The hair on one side of the animal was removed by cutting with scissors (the skin was not shaved). A definite amount (5 drops) of the following dilutions of croton oil in olive oil was dropped on the skin, 1 : 5, 1 : 10, 1 : 20 (in some experiments), 1 : 30, 1 : 50. A 10 per cent. solution of turpentine in olive oil was also employed. Twenty-four hours later the reaction resulting from such applications was noted and expressed in the following manner: A + + + reaction (the greatest reaction observed) consisted of an edematous, raised, markedly erythematous lesion, the surface of which invariably became moist, slightly crustaceous, and, still later, scaly. A + + reaction consisted simply of marked erythema. A + reaction consisted of erythema much less in degree, as manifest in color, than in the preceding reaction. A ± reaction consisted of just appreciable erythema (slight pink).

After the cutaneous reaction resulting from the foregoing applications was recorded, experimentation was instituted, following which,

8. The cutaneous reaction to external irritation is approximately of the same character in the rabbit as in the cat. Since rabbits are more conveniently handled than cats, the former animals were employed in almost all of the experiments.

the other side of the animal was similarly dealt with. The cutaneous reaction resulting from this second application was compared with the cutaneous reaction resulting from the first or control reaction.

With the exception of the dietary experiments, a mixed diet was administered throughout the experiments. In the experiments involving the injection of certain drugs, the cutaneous tests were applied twenty-four hours after such injection. Exceptions to this will be mentioned later.

In some instances, the animal was discarded after one experiment. In most instances, however, the animal was placed on a mixed diet in the dietary experiments, and in other experiments the mixed diet was continued, and after a variable period, as shown in the tables, the skin was again tested prior to another experiment.

The aforementioned technic was employed in those experiments in which the cutaneous sensibility of cats was studied.

CUTANEOUS SENSIBILITY OF RABBITS UNDER NORMAL CONDITIONS

A considerable variation was observed in the cutaneous reaction of rabbits, under normal conditions, to the dilution of croton oil employed. Some animals reacted only to the 1 : 5 dilution, others reacted in a variable degree to all dilutions employed. In exceptional instances, the animal did not react to any of the dilutions. This variability of the cutaneous reaction in animals under normal conditions could not be correlated with the sex, age or color of the animal. Generally, white rabbits did not react in a greater degree than did dark colored or black rabbits. However, it was definitely observed that pigmented areas, regardless of the color of the animal, reacted considerably less or not at all to the dilution that called forth a much greater reaction in the adjacent nonpigmented skin.[9]

No variability of the cutaneous reaction was observed in the same animal under normal conditions. Animals on a mixed diet tested for cutaneous sensibility in the foregoing manner and retested one or more times at variable periods, a week or longer, reacted to each test in much the same manner.

The skin at the site of a + + + and a + + reaction, less likely with a + reaction, became scaly and dry before becoming entirely normal. At this time, the same area of skin, if again tested, would invariably react in the same degree as before. Constantly applied

9. This observation is in accordance with clinical observation referable to the protection skin pigment affords against external irritation, actinic or chemical, and to the lesser incidence of dermatitis venenata, and indeed eczema, in negroes than in white persons.

chemical irritation (the dilutions of croton oil employed) at the same site would result in a dry condition of the skin, with scale formation and some fissuring. The condition would remain unchanged for some time, but would disappear eventually, and the skin would become normal. This phenomenon is somewhat analogous to a state of chronic eczema.

EXPERIMENTS

Forty-four rabbits were employed throughout the study. The experiments referable to diet consisted of feeding all oats, green fodder (mostly kale and spinach, some cabbage and carrots and carrot leaves), boiled hominy (diet high in carbohydrate), tankage (diet high in protein) and whole buckwheat [10] (an endeavor to photosensitize the skin of the rabbit). The animal was maintained on one or the other of these diets for ten days, in some instances for one week.

The effect on cutaneous sensibility was studied after removal of the spleen, almost complete removal of the pancreas and removal of one and of both suprarenals. Different rabbits were employed in these experiments.

An experimental nephritis in rabbits was produced by an intramuscular injection of 0.015 gm. per kilogram of uranium acetate followed in twelve days by an injection of 0.020 gm. per kilogram. The animal died of an acute nephritis. An experimental hepatitis was produced by an intramuscular injection of 0.2 c.c. per kilogram of chloroform in olive oil, followed by an injection of 0.4 c.c. per kilogram nine days later and 0.6 c.c. per kilogram sixteen days later. Twenty-four hours after the latter dose, the animal died. Histologic sections of the liver showed an acute atrophic hepatitis.

The following drugs were injected intramuscularly into rabbits: Calcium chlorid was employed in a 3 per cent. solution, in daily doses of about 10 c.c. The total number of cubic centimeters injected varied from 24 c.c. to 60 c.c. All animals injected with more than 24 c.c. died of nephritis. Tenth normal hydrochloric acid was injected in daily doses of 10 c.c. up to a total of 80 c.c. Two animals received injections; one died after receiving this amount.

A 3 per cent, solution of oxalic acid was injected in daily doses of 5 c.c. for five injections. The animal died.

The following drugs were injected subcutaneously: Two injections of a 10 per cent. solution of starch in daily doses of 8 c.c.; three consecutive injections of a 2 per cent. solution of gelatin in daily doses of

10. An attempt was made to feed a rabbit exclusively on cream (a high fat diet) with the stomach tube. This was not successful, and the experiment was discontinued.

2 c.c and a fourth injection of 6 c.c. At this time skin tests were performed. Two injections of a 5 per cent. solution of sodium sulphate were given in daily doses of 10 c.c.

Arsenic was administered in the form of neo-arphenamin. A sublethal dose, 0.2 gm. per kilogram, was injected intravenously into a rabbit. Forty-eight hours later, skin tests were performed. Sterile distilled water, 0.2 c.c., was injected intravenously and the injection repeated in two days; daily injections were given for four consecutive days in another experiment. Milk, 0.3 c.c., was injected intramuscularly for three successive days, and a single injection of 0.4 c.c. was given intramuscularly in another rabbit. Three fourths cubic centimeter was also injected intracutaneously into two different cats. Skin tests were applied three days after the intracutaneous injections and twenty-four hours after the intramuscular injections. Human serum, 0.75 c.c., was injected intracutaneously into a cat, and 1.5 c.c. was injected intramuscularly into a rabbit. Skin tests were performed three days after these injections. Pooled serum, totaling 40 c.c., from three patients with acute generalized eczema was injected intraperitoneally in a cat. Twenty-five cubic centimeters of serum from another patient with acute generalized eczema was also injected intraperitoneally in two daily doses into another cat. Skin tests were performed twenty-four hours after the last injection.

The effect of deep narcosis on cutaneous sensibility in a rabbit was studied in the following manner: Chloral hydrate, a total of 1 gm. per kilogram, was administered by rectum in divided doses over a period of six hours. The animal receiving the injections was deeply narcotized (corneal reflex lost) during this time.

Following many of the foregoing experiments, the animal lost more or less in weight. The loss in the majority of animals ranged from 100 to 300 gm. As a control experiment directed at this loss in weight, the effect of starvation on cutaneous sensibility was studied. In this experiment, food was withheld from a rabbit, water only being allowed for one week. During this period the animal lost 200 gm. There was no change in cutaneous sensibility.

BLOOD CHEMISTRY STUDIES

In many experiments, the nonprotein nitrogen, urea nitrogen, sugar and calcium content of the blood was determined prior and subsequent to the experiment conducted. In this way, the amount of these ingredients in the blood of the rabbit under normal conditions (mixed diet) was obtained. In later experiments, blood chemistry studies were conducted only after the experiment. The blood chemistry picture at this time was compared to what was previously determined as the normal picture. It was observed that under normal conditions the nonprotein

nitrogen ranged from 30 to 40 mg. per hundred cubic centimeters of blood;[11] the urea nitrogen from 10 to 20 mg.; the sugar from 80 to 125 mg., and calcium from 10 to 12 mg.

The results of these studies are shown in the tables. It will be observed that the changes in the nonprotein, urea nitrogen and sugar content of the blood before and after the dietary experiments were slight, and within normal variations and those due to technical error. The change in calcium content was likewise slight and within normal limits.[12] However, generally the change in calcium content, although slight, was in the expected direction. Thus, as shown in Table 1, after

TABLE 1.—*Variation in Sensibility of Skin of Rabbit After Green Fodder Diet, Oat Diet, Mixed Diet, Injection of Human Serum and Injection of Hydrochloric Acid*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil					Blood Chemistry			
Date	Experiment	1:5	1:10	1:30	1:50	10% Turpentine	Nonprotein Nitrogen	Urea Nitrogen	Sugar	Calcium
1/ 5	Before experiment, animal on mixed diet *	++	++	+	+	+‡	32	15	97§	....
1/15	After 10 days of green fodder;† lost 330 gm. in weight	++	+	±	—	—	34	17	90	10.9
1/29	After 10 days of oat diet; lost 60 gm.	++	++	+	+	+	..	..	..	10.1
2/ 4	After 5 days of mixed diet	++	++	+	+	+	..	..	..	....
2/23	After two daily intramuscular injections of 15 c.c. of human serum; mixed diet continued	+	+	±	—	—	..	..	..	....
2/29	Six days later	++	++	+	+	+	..	..	..	....
3/22	After intramuscular injection of 80 c.c. of tenth normal hydrochloric acid in doses of 10 c.c. daily	++	++	+	+	+	..	..	..	9.4
3/27	Lost 600 gm. in weight; paralysis of hind legs; death									

* Beet pulp, oats, hay, greens and bread.
† Mostly kale and spinach, some cabbage and carrots.
‡ +++ reaction; an edematous, raised markedly erythematous lesion. ++ reaction; marked erythema. + reaction; erythema, less than preceding. ± reaction; very slight erythema.
§ These figures, as well as those in the other tables, are milligrams per hundred cubic centimeters of blood.

an all green diet, the calcium was 10.9; the same rabbit when fed on an all oat diet showed a calcium content of 10.1, and still later after injections totaling 80 c.c. of hydrochloric acid, the calcium content was 9.4. On the other hand, in another rabbit (experiment not tabulated), after injections totaling 60 c.c. of hydrochloric acid, the calcium content was 11.3. The most marked change observed in the entire study is shown

11. All subsequent figures are milligrams per hundred cubic centimeters of blood.

12. Rockwood, R., and Barrier, C. W.: Calcium Treatment for Edema, Arch. Int. Med. **33**:643 (May) 1924, observed that the calcium content of the blood remained unchanged in patients in whom as much as from 8 to 12 gm. of calcium chlorid or lactate was administered by mouth for some time.

in Table 3 (Rabbit 10). After an oat diet, the calcium content was 7.2; after injections of calcium chlorid, oat diet continued, it arose to 8, and still later, after a mixed diet, it was 8.4. In this experiment the cutaneous sensibility was increased after an oat diet and decreased after injections of calcium chlorid. In some of the experiments, when the cutaneous sensibility decreased, as after an all green diet and after injections of calcium chlorid, the calcium content arose, and conversely, when the cutaneous sensibility increased, as after an oat diet, the calcium content decreased. On the other hand, cutaneous sensibility increased after a tankage diet (Table 2, Rabbit 20), whereas the calcium content arose from 10.5 to 11.1. On the whole, the state of cutaneous sensibility could not be correlated with blood chemistry studies, particularly the calcium content of the blood.

TABLE 2.—*Results of Study of Sensibility of Skin of Rabbits After High Protein Diet (Tankage) Starvation, Buckwheat Diet, Green Fodder Diet*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil					Blood Chemistry				
Date	Experiment	1:5	1:10	1:30	1:50	10% Turpentine	Non-protein Nitrogen	Urea Nitrogen	Sugar	Calcium	Magnesium
Rabbit 20; male; black and white; weight, 1,695 gm.											
2/ 1	Before experiment; animal on mixed diet*	+	+	—	—	—	34	16	106	10.5	...
2/15	After 10 days of tankage diet†	++	++	+	+	—	32	16	102	11.1	...
Rabbit 25; male; gray; weight, 1,715 gm.											
2/28	Before experiment	+++	+++	+	+	+	30	15	97	10.9	2.2
3/14	After 1 week of starvation; water only (not distilled); lost 200 gm. in weight	+++	+++	+	+	+	..	..	...	....	...
3/15–21	Mixed diet	....	....	..	..	..	..	..	...	....	...
3/31	After 10 days of whole buckwheat diet; gained 155 gm.	+++	+++	+	+	+	..	..	...	10.2	...
4/15	After 10 days of green fodder†	++	+	±	±	—	..	..	...	11.2	...

* Beet pulp, oats, hay, greens and bread.
† Mostly kale and spinach, some cabbige and carrots.

RESULTS OF EXPERIMENTS [13]

Diet Experiments.—As shown in Table 1, there was a definite decrease in cutaneous sensibility after the animal was fed on all greens for ten days. In another experiment, however, the decrease was much less definite (Table 2, Rabbit 25). There was an appreciable though

13. In the interpretation of the results, it is important to bear in mind the possible error in making a comparison of a degree of cutaneous reaction mostly manifested by degree of erythema, which is evidenced by color. This of course applies to slight changes but does not apply to instances in which one or more of the dilutions employed produced no cutaneous reaction prior to experimentation but did subsequently. In these instances, therefore, error in reading the tests can be excluded.

not a striking increase in cutaneous sensibility after ten days of oat diet, as shown in Tables 1 and 3 (Rabbit 10). There was a definite increase in cutaneous sensibility after tankage diet (Table 2, Rabbit 20) and after hominy diet (Table 3, Rabbit 22). Cutaneous sensibility, however, remained unchanged after a buckwheat diet and after one week of starvation (Table 2, Rabbit 25).

TABLE 3.—*Results of Study of Sensibility of Skin of Rabbits After the Following: Oat Diet, Injection of Calcium Chlorid, Hominy Diet, Injection of Calcium Chlorid*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil					Blood Chemistry					
Date	Experiment	1:5	1:10	1:30	1:50	10% Turpentine	Non-protein Nitrogen	Urea Nitrogen	Sugar	Calcium	Magnesium	Creatinin
Rabbit 10; female; gray; weight, 1,900 gm.												
12/28	Before experiment; animal on mixed diet*	++	++	+	—	—	37	17	107	....	...	..
1/15	After 10 days of oat diet; no loss in weight	++	++	++	+	—	35	17	99	7.2	...	..
1/21	After intramuscular injection of 24 c.c. of 3 per cent. solution of calcium chlorid in doses of 8 c.c. daily; oat diet continued	+	+	±	—	—	..	..	...	8.0	...	..
2/ 8	After 16 days of mixed diet	+	+	—	—	—	..	..	...	8.4	...	..
Rabbit 22; male; black; weight, 2,250 gm.												
2/12	Before experiment; animal on mixed diet	+++	++	+	+	—	35	17	99	11.0	2.3	..
3/ 9	After 10 days of boiled hominy diet; lost 350 gm. in weight	+++	+++	++	++	+	34	16	103	10.6	2.2	..
3/18	After 50 c.c. of 3 per cent. solution of calcium chlorid injected intramuscularly in daily doses of 10 c.c.; lost 400 gm.	++	++	—	—	—	240	168	...	9.9	2.3	7
3/19	Animal died; nephritis †											

* Beet pulp, oats, hay, greens and bread.

† The blood chemistry picture in this animal evidenced a nephritis. In other animals, receiving injections of approximately the same amount of calcium chlorid, histologic examination of the kidney showed a marked albuminous and early fatty degeneration of the tubular epithelium.

Injection of Calcium Chrolid.—As shown in Table 3 (Rabbit 22) and 4 (Rabbit 40), there was a striking decrease in cutaneous sensibility following injections of calcium chlorid, from which the animal succumbed.[14] The decrease was much less striking in another experiment

14. The lethal dose of calcium chlorid in rabbits is 5 c.c. per kilogram of a 3 per cent. solution injected intramuscularly daily for from four to six days. In the animals receiving injections with this amount, the blood chemistry picture evidenced nephritis. In those in which histologic sections of the kidney were made, a marked albuminous and early fatty degeneration of the tubular epithelium was seen.

(Table 3, Rabbit 10) in which a smaller amount of calcium chlorid was injected (the animal survived). In these experiments, it will be noted that injections of calcium chlorid were made while the animals were maintained on a mixed diet in two instances and on an oat diet in another instance.

Injection of Acids.—Daily injections of tenth normal hydrochloric acid and of a 3 per cent. solution of oxalic acid, which killed the animal, did not alter cutaneous sensibility (Tables 1 and 4, Rabbit 37). In another experiment (not tabulated), in which a total of 80 c.c. of hydrochloric acid was injected, cutaneous sensibility was not altered.

TABLE 4.—*Sensibility of Skin of Rabbits Decreased After Injection of Calcium Chlorid and Unchanged After Injection of Oxalic Acid*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil						Blood Chemistry				
Date	Experiment	1:5	1:10	1:20	1:30	1:50	10% Turpentine	Non-protein Nitrogen	Urea Nitrogen	Sugar	Calcium	Creatinin
Rabbit 40; male; tan; weight, 2,200 gm.												
3/17	Before experiment; animal on mixed diet *	+++	+++	++	++	++	+	..	..	...	....	...
3/24	After intramuscular injection of 40 c.c. 3 per cent. solution of calcium chlorid in daily doses of 10 c.c.; (mixed diet continued); animal died; nephritis; lost 350 gm. in weight	++	+	—	—	—	—	60	49	163	11.9	3.8
Rabbit 37; male; gray; weight, 1,535 gm.												
4/ 2	Before experiment; animal on mixed diet	++	++	—	—	—	—	..	..	...	....	...
4/ 8	After intramuscular injection of 25 c.c. of 3 per cent. solution of oxalic acid; (mixed diet continued); lost 100 gm.	++	++	—	—	—	—	..	..	...	11.2	...
4/11	Animal died											

* Beet pulp, oats, hay, greens and bread.

Experimentally Produced Nephritis and Hepatitis.—There was a striking increase in cutaneous sensibility after the production of nephritis and hepatitis. These results are shown in Table 5 (Rabbit 30). It is interesting to note that increased cutaneous sensibility apparently preceded the blood chemistry picture of nephritis. In the case of the hepatitis experiment (Rabbit 32), the initial increase in cutaneous sensibility was noted after the first injection of chloroform.

Removal of Spleen, Pancreas and Suprarenals.—Cutaneous sensibility remained unchanged after the removal of the spleen. It likewise was unchanged after the removal of from one half to three

fourths of the pancreas. In this experiment, cutaneous tests were applied on the second and third day. Sugar was present in the urine.

Both suprarenal glands were removed from a number of rabbits. These animals did not survive the shock of the operation; death occurred at varying periods up to about ten hours after the operation. Until the death of the animals, there was no change in cutaneous sensibility. One animal, however, lived ten days after the removal of both glands. Unfortunately, in this animal cutaneous tests were not performed prior to the operation. The reaction to tests applied at varying periods after the operation were such that it could be regarded as an average reaction; moreover, there was no heightening in the reac-

TABLE 5.—*Increased Sensibility of Skin of Rabbits After Experimentally Produced Nephritis and Also Hepatitis*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil					Blood Chemistry			
Date	Experiment	1:5	1:10	1:30	1:50	10% Turpentine	Non-protein Nitrogen	Urea Nitrogen	Creatinin	Bilirubin
Rabbit 30; female; white, brown spots; weight, 1,865 gm.										
3/25	Before experiment; animal on mixed diet *	++	—	—	—	—	..	..	..	..
3/28	Intramuscular injection of 15 mg. per kilogram of uranium acetate									
4/ 4	Mixed diet continued throughout experiment	+++	++	—	—	—	38	18	..	..
4/ 9	Intramuscular injection of 20 mg. per kilogram of uranium acetate									
4/13		+++	+++	+	+	+	260	150	..	7
4/14	Died; nephritis; lost 300 gm. in weight									
Rabbit 32; male; tan; weight, 2,713 gm.										
3/25	Before experiment; animal on mixed diet	+	—	—	—	—	..	..	..	..
3/30	Intramuscular injection of 2 c.c. per kilogram of chloroform in olive oil									
4/ 4	Mixed diet continued throughout experiment	+	+	—	—	—	..	..	..	Neg.
4/ 8	Repeat injections of 6 c.c. per kilogram of chloroform									
4/14		++	++	+	±	±	..	..	..	Neg.
4/15	Repeat injections of 6 c.c. per kilogram of chloroform									
4/16	Died; lost 313 gm. in weight; necropsy, acute atrophic hepatitis									

* Beet pulp, oats, hay, greens and bread.

tion of these tests compared to one another. In another animal, one gland was removed, followed in five days by the removal of the other. Twenty-four hours after the removal of the first gland, cutaneous sensibility was unchanged; it was likewise unchanged at the same period after the removal of the second gland.[15]

15. The two animals which survived the operation of removing both glands were previously castrated. In both animals, necropsy disclosed a complete absence of both suprarenal glands. Peritonitis was present in both.

Narcosis.—The decrease in cutaneous sensibility as a result of narcosis was striking. Cutaneous tests were applied immediately after the animal was narcotized. Narcosis continued for six hours. After recovery, there was no heightening of the cutaneous reaction. The estimated decrease in cutaneous sensibility was perhaps greater than 50 per cent. (This experiment is not tabulated.)

Injections of Human Serum and Serums of Patients with Eczema.—There was a definite decrease in cutaneous sensibility after intramuscular as well as intracutaneous injections of human serum (Tables 1 and 4). Cutaneous sensibility was not increased, but, on the contrary, decreased after intraperitoneal injections into two cats of serums from patients with acute generalized eczema. The result of one of these experiments is shown in Table 6.

TABLE 6.—*Decreased Sensibility of Skin of Cat After Injection of Human Serum and Also Milk, Unchanged After Injection of Serum of Patient with Acute Eczema*

		Reaction of Skin to Croton Oil, Diluted in Olive Oil				
Date	Experiment	1:5	1:10	1:30	1:50	10% Turpentine
2/ 4	Before experiment *	+++	+++	++	+	—
2/18	Three days after intracutaneous injection of 0.75 c.c. of human serum	+++	++	—	—	—
2/27	Ten c.c. of serum of patient with acute eczema, injected intraperitoneally					
3/ 3	Fifteen c.c. of same serum similarly injected					
3/ 4		+++	++	—	—	—
5/12		+++	++	+	+	+
5/17	Three days after intracutaneous injection of 0.75 c.c. of sterile milk	+++	++	—	—	—

* Same diet before and during experiment.

Injections of Milk and of Sterile Water.—The results in these experiments were conflicting. One cat receiving intracutaneous injections with milk showed a definite decrease in cutaneous sensibility three days after the injection (Table 4); in another cat, there was only a slight decrease. Twenty-four hours after intramuscular injections in two different rabbits, cutaneous sensibility was unchanged. There was a definite increase in cutaneous sensibility in a rabbit after the intravenous injection of sterile water. The injection was repeated in two days, at which time skin tests were performed. In another experiment, however, cutaneous sensibility remained unchanged after four consecutive daily intravenous injections of sterile water.

Injections of Starch, Gelatin and Sodium Sulphate.—There was a definite decrease in cutaneous sensibility after injection of gelatin. The cutaneous sensibility remained unchanged after injections of starch and of sodium sulphate.

Injection of Arsenic (Neo-arsphenamin).—A definite, but not a striking, increase in cutaneous sensibility was observed after an injection of a sublethal dose of neo-arsphenamin.

The results of many, but not all, of the foregoing experiments are shown in Tables 1 to 6. Such results are representative of the results obtained in the entire study.

DISCUSSION OF EXPERIMENTS

Our results were not in entire accord with those of Luithlen, particularly since we failed to increase the irritability of the skin by injections of hydrochloric acid and of oxalic acid. These drugs were injected for the purpose of disturbing the metabolism of bases, which Luithlen assumes plays an important rôle in altering cutaneous sensibility. Our observation on the calcium content of the blood in the study herein reported did not evidence a state of demineralization of the animal. However, the calcium content of the blood is probably no index of the ionic activity of the dermal cells.[16]

The results of our studies could not establish a definite relationship between the calcium content of the blood and alterations in cutaneous sensibility. However, our observations on cutaneous sensibility after an all green diet (rich in bases), after an all oat diet (poor in bases) and after injections of calcium chlorid were significant of the rôle played by the metabolism of bases in altering cutaneous sensibility.

The extent of our studies did not warrant the definite conclusions of Luithlen.[17] However, it must be emphasized that our studies were limited so far as they concerned the metabolism of bases.

The metabolism of bases is perhaps not the sole factor in altering cutaneous sensibility. There is evidence of other causes. For example, the altered sensibility of the skin under narcosis is probably not concerned with biochemical changes involving the bases.

The altered sensibility of the skin resulting from diet and from other causes observed in our study is doubtless intimately concerned with physiochemical changes in the dermal cells, thus changing their reaction capacity. Altered reactibility of the skin, like nearly every symptom of disease, in all probability evidences pathologic physiologic cellular changes. The metabolism of inorganic salts is just as important as the metabolism of protein, carbohydrate and fat in maintaining physiologic equilibrium of the ionic cell content. There are other controlling factors, at present imperfectly understood, in maintaining equilibrium

16. It is well known that although the calcium content of blood is normal in patients with rickets, yet there is a derangement in the metabolism of calcium.

17. In Luithlen's study (footnote 7), which concerned the content of the skin in bases after an all green and an all oat diet and after the injection of acids, the differences observed, in some instances, were within the limits of experimental error, and perhaps did not warrant such definite conclusions.

of physiochemical cell function. Nerve action and the glands of internal secretion are apparently vital correlating factors.

Viewed in its broadest aspects, the work of Luithlen is pioneer in the direction of a physiochemical conception of certain skin diseases. The final analysis in the pathogenesis of symptoms of disease generally may eventually be expressed in terms of biochemistry of the cell but not until future investigations clarify imperfectly understood phenomena of colloidal chemistry.

There is a paucity of knowledge relative to the chemistry of the skin. In view of the work of Luithlen, it is interesting to note that Klose [18] in an investigation of the chemical composition of different parts of the body in new-born infants reports the results of his research on the skin from the back of nineteen infants. From this study, he concludes that the skin seems to be the first part of the body called on to store water in pathogenic conditions, and it is also active in mineral metabolism, storing and eliminating mineral substances independent of the water metabolism.

On the other hand, Wilson [19] in his extensive study of the chemistry of the skin of animals enumerates only sulphur and phosphorus as among the inorganic constituents. Our studies of the chemistry of the skin following different diets will be reported later.

It is well known that inorganic salts, calcium, magnesium, sodium and potassium are of considerable importance to cellular activity. It appears that calcium is one of the most important.

According to the experimental observations of others,[20] calcium modifies the phenomenon of inflammation by decreasing the permeability of the cells of the tissues. If this is true [21] it may in part explain its action in decreasing the reactibility of the skin.

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18. Klose, E.: Zur Kenntnis der Korperzusammensetzung bei Ernährungsstörungen. Der chemismus der Haut bei Ernährungsstörungen, Jahrb. f. Kinderh. **91**:157-181, 1920.

19. Wilson, J. A.: The Chemistry of Leather Manufacturing, New York Chemical Catalogue Co., Am. Chem. Soc. Monograph ser., 1925, p. 65.

20. Januschke, H.: Ueber Entzundungshemmund, Wien klin. Wchnschr. **26**:869-874, 1913.

21. Cushing: ("Pharmacology and Therapeutics," Ed. 8, 1914, p. 565), however, states the following: "There is some not altogether convincing evidence that lime salts lessen the permeability of the cells of the tissues; for example, it is stated that in the presence of traces of calcium, dried cells take up less water." This view has been further developed by Chiari and Januschke, who state that when an animal has been treated with lime salts the intravenous injection of iodids does not induce pleural effusion and edema, while it has this effect in untreated animals; the statement that strong irritants may be applied to the conjunctiva without swelling and effusion in these treated animals is certainly erroneous, as was shown repeatedly in experiments on the poison gases during the Great War. The whole theory of the specific action of calcium on effusion and inflammation requires further investigation before it can be accepted.

Pottenger,[22] from theoretical consideration, regards calcium as a sympathetic nerve stimulant, and successfully employs it in the treatment of many parasympathetic syndromes. He calls attention to the importance of the sympathetic nerves in their relationship to all dermal and subdermal structures and to the fact that affections of the skin accompanied by itching should be considered in their relationship to the sympathetic neurocellular mechanism.[23] He mentions the relationship of protein foods to calcium and states that protein foods are broken down into certain acids which combine with calcium and cause its rapid elimination. He believes that the reason why patients suffering from asthma and eczema and other diseases of this type do best on a low protein diet is now furnished with a physiologic explanation.

Buckwheat was the only dietary experiment in which no alteration in the sensibility of the skin was observed. The purpose of this experiment was directed at an attempt to photosensitize the skin. After ten days of this diet, the animal was exposed to the sun during an entire day. Negative results were obtained. It is appropriate to recall here that cattle, pigs and sheep when fed on either the buckwheat plant or kernel develop photosensitivity of the skin.[24]. Only light colored animals, as well as the nonpigmented spots in dark colored, animals are affected.

The marked decrease in the sensibility of the skin as a result of narcosis manifests the rôle of nerve action in influencing the phenomenon of effusion and inflammation.

Eczema is an inflammatory reaction of the skin. In a consideration of its pathogenesis, it is appropriate to review briefly the work of Bruce,[25] Januschke and Chiari and Januschke[26] relative to conditions which they observed modified the phenomena of effusion and inflammation. It was observed that the inflammatory reaction following the instillation of mustard oil in the conjunctiva of rabbits could be prevented or greatly modifled by the following procedures: cutting the

22. Pottenger, F. M.: The Relationship of the Ion Content of the Cell to Symptoms of Disease, with Special Reference to Calcium and Its Therapeutic Application, Ann. Clin. Med. **2**:187-196 (Nov.) 1923.

23. The relationship between the parathyroids, possibly the thyroid and anterior lobe of the pituitary, and calcium metabolism may serve to explain the beneficial results obtained, in some instances, by the use of these glands in the treatment of certain skin diseases.

24. Hausmann, Walther: Grundzüge der Lichtbiologie und Lichtpathologie, Berlin, 1923, p. 150.

25. Bruce, A. N.: Ueber die Beziehung der sensiblen Nervenendigungen zum Entzündungsvorgang, Arch. f. exper. Path. u. Pharmakol. **63**:424-433, 1910.

26. Chiari, R., and Januschke, H.: Hemmung von Transsudat. und Exsudatbildung durch Kalziumsalze, Arch. f. exper. Path. u. Pharmakol. **65**:120-127, 1911.

trigeminus nerve, a prior instillation of local anesthetics, narcosis of the animal induced by ether, as well as a number of other anesthetics. After recovery from narcosis, the conjunctiva promptly reacted to mustard oil instillation. A subcutaneous injection of a solution of epinephrin prevented the reaction, although the vessels of the conjunctiva were bloodless. The administration of antipyrin, quinin or magnesium chlorid modified but did not prevent reaction.

Luithlen [27] noted a decrease in the sensibility of the skin after the injection of homologous and heterologous serums, and to a less extent after the injection of colloidal substances, and an increase after the injection of certain electrolytic substances such as sodium sulphate. He attributed these changes to complex alterations in the tissues, of a colloidal nature. Our results in the foregoing were in a general way similar to those obtained by Luithlen. An exception, however, was the negative results obtained after the injection of starch solution and sodium sulphate.

The beneficial results at times obtained in foreign protein therapy of skin diseases may partly be explained by the foregoing observation. In this regard, the effects of milk injections and intravenous injections of sterile water on cutaneous sensibility was studied. After injection of milk, we observed some evidence of decreased cutaneous sensibility.

The increase in the sensibility of the skin after the administration of a sublethal dose of neo-arsphenamin is probably concerned with an increased permeability of vessels incident to the well-known vasculotoxic action of arsenic.[28] This observation is somewhat consistent with clinical observation relative to the harmful influence large doses of arsenic exert on an acute generalized dermatosis. This is particularly true in cases of acute psoriasis.

The experiment involving a double suprarenalectomy is to be regarded only as a partial suprarenalectomy in view of the presence in

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27. Luithlen, F.: Veränderungen der Hautreaktion bei Injection von Serum und kolloidalen substanzen, Wien. klin. Wchnschr. **26**:653-658, 1913.

28. Large areas of erythema were produced on the skin of rabbits with formaldehyd. In the subsiding stage of this reaction, a sublethal dose of neo-arsphenamin was administered to the animal. Following this treatment, the areas of erythema were observed for an exacerbation. The experiment was negative. An attempt was thus made to produce a somewhat analogous phenomenon observed clinically which concerns an accentuation of seborrheic dermatitis as the beginning of postarsphenamin dermatitis. Hoppe and Schreiber studied the vasotrophic action of arsphenamin. It was observed that this action is more marked in organs that are at first artificially damaged. These studies suggested another explanation of the Herxheimer reaction, which concerns the vasotrophic action of arsenic. Klauder, J. V.: The Clinical Aspects of Cutaneous Reaction After Arsphenamin, J. A. M. A. **82**:933-939 (March 22) 1924.

probably all rabbits of accessory cortical tissue.[29] Although the results of this experiment in which cutaneous sensibility was unchanged,[30] is not conclusive, it is worthy of comment in view of the function of the suprarenals relative to vasomotor stability. Futhermore, Bell [31] observed that in rabbits in which one suprarenal gland was removed, a considerable increase in the urinary excretion of calcium occurred. In one animal, the average quantity excreted after operation was seven times as much as that excreted before operation; in the other animal, it was more than sixteen times as much. These findings, although based on only two animals studied, suggest a disturbance in calcium metabolism.

Both rabbits in our study were previously castrated before the removal of the suprarenal glands. In this connection, it is of interest to note that Bell and Hick [32] observed that castration prevented tetany in cats from which the thyroid with most of the parathyroidal tissue had been removed. Bell states that in these circumstances, it is possible that a considerable calcium retention is produced, for apparently the parathyroids and gonads, especially the ovaries, are antagonistic to the calcium metabolism.

Further experiments are being conducted relative to the influence the suprarenals and other hormonopoietic organs exert in altering cutaneous sensibility.

SUMMARY

It has been demonstrated by others that the skin of patients with eczema is in an increased state of sensibility. The experimental work of Luithlen in the direction of determining conditions that alter the sensibility of the skin of rabbits and cats is reviewed. Luithlen concludes that the metabolism of bases plays an important rôle in altering the sensibility of the skin.

In our study, rabbits were mostly employed, also cats. Prior to experimentation (the animals on a mixed diet) a definite amount of different dilutions of croton oil in olive oil and a 10 per cent. solution of turpentine in olive oil was applied to the skin of one side of the ani-

29. According to Marine and Baumann (J. Metabolic Res. **1**:777 [June] 1922), accessory cortical tissue is probably present in all rabbits and is readily demonstrated in about 70 per cent. The varying lengths of time that rabbits survive extirpation of the suprarenals is believed to depend on the presence of varying amounts of accessory cortical tissue.

30. It is interesting to recall here the uncompleted experiments of the late Dr. Frederick S. Harris (The Etiology of Eczema, Arch. Dermat. & Syph. **3**:579-592 [May] 1921) in the direction of determining diminished epinephrin in the blood of patients with eczema as a possible cause of the increased sensibility of the skin.

31. Bell, W. B.: The Sex Complex, Ed. 2, London, 1920, p. 76.

32. Bell, W. B., and Hick, P.: Observations on the Physiology of the Female Genital Organs, Brit. M. J. **1**:517-522, 1909.

mal. The reaction thus caused (expressed in terms of ± to +++) was compared to the reaction resulting from a similar application on the untreated side of the same animal after experimentation. There was a considerable variation in the cutaneous reaction of different animals, under normal conditions, to the aforementioned applications. No variation in the cutaneous reaction to these applications was noted in the same animal, under normal conditions examined at varying intervals.

The following experiments were conducted: Diets consisting exclusively of greens, oats, hominy, tankage and buckwheat were given. The effect of starvation was observed. Varying amounts of the following were injected—tenth-normal hydrochloric acid, 3 per cent. oxalic acid, human serum and the pooled serums of patients with acute eczema, milk, sterile water and varying dilutions of solutions of starch, gelatin and sodium sulphate. The effect of arsenic (a sublethal dose of neo-arsphenamin) and also narcosis by chloral hydrate was observed. The effect of removal of the spleen, suprarenals, and partial removal of the pancreas was also observed, as well as the effect of an experimentally induced nephritis and hepatitis.

Blood chemistry studies with particular reference to the calcium content of the blood were correlated with the results of the aforementioned experiments. Slight variations within normal limits were observed in the blood chemistry studies. On the whole, the state of cutaneous sensibility could not be correlated with blood chemistry studies, particularly the calcium content of the blood.

Cutaneous sensibility was altered by diet, decreased after all greens and increased following other diets employed, with the exception of buckwheat. After the latter diet, cutaneous sensibility remained unchanged. Attempts to photosensitize the skin by the buckwheat diet were unsuccessful. There was a striking decrease in cutaneous sensibility following injections of calcium chlorid. Cutaneous sensibility remained unchanged after lethal and sublethal injections of hydrochloric and oxalic acids, after removal of the spleen, pancreas and suprarenals. Experimentally induced hepatitis and nephritis increased the sensibility of the skin. There was a striking decrease as a result of narcosis. Most of the colloidal substances injected, including human serum and serums of patients with acute eczema, decreased cutaneous sensibility. A sublethal dose of neo-arsphenamin increased cutaneous sensibility.

The results of these experiments have been discussed with particular reference to the rôle played by the metabolism of bases in altering cutaneous sensibility.

It was concluded that cutaneous sensibility of rabbits and cats was altered by diet, injection of drugs and colloidal substances, by narcosis and by injuring certain viscera; that some evidence was obtained to prove

that metabolism of basic substances, particularly calcium, plays a rôle in determining altered sensibility of the skin. It further appears from our observations and the evidence reviewed that other factors are concerned in addition to the metabolism of bases.

The results of most of the experiments are shown in tables.

CONCLUSIONS

Cutaneous sensibility of rabbits and cats was altered by diet, injection of drugs and colloidal substances, by narcosis and by injuring certain viscera (experimentally produced nephritis and hepatitis). Such altered cutaneous sensibility could not definitely be correlated with blood chemistry studies with particular reference to the calcium content of the blood. However, we obtained some evidence that metabolism of basic substances, particularly calcium, plays a rôle in determining altered sensibility of the skin. It further appears from our observations and the evidence reviewed that other factors are concerned in addition to the metabolism of bases.

DISCUSSION

Dr. Jay Frank Schamberg, Philadelphia: Dr. Klauder has brought to us a piece of work based on assiduous investigation carried out over many months, the results of which I think are extremely interesting.

The salient points that he emphasizes, from my interpretation of his communication, are these: First, that rabbits under the influence of a diet rich in albumin will react very much more definitely to standardized external irritation than rabbits on green fodder diet.

In the second place, animals to which salts of calcium are given acquire a decreased sensibility to irritation of the skin. In connection with this, there are reports coming from Germany in which reference is made to the use of calcium salts in certain dermatoses. Dr. Klauder calls attention to the fact that calcium salts introduced by the blood stream are quite toxic, and this must be considered. We have been employing calcium salts, particularly in eczema, and while our primary impressions are favorable, we can make no positive statements.

Another point is that the experimental production of nephritis, confirmed by necropsy and by chemical blood studies and degenerative changes induced in the liver, distinctly increase the susceptibility of the skin to irritants. I think that it is important and in line with deductions from other chemical blood studies. The finding is interesting in connection with the opinion expressed by Mr. Brown and myself, that renal dysfunction is at the bottom of many cases of eczema in adults.

Finally, I wish to refer to the findings with respect to the inorganic salts in eczema. Some recent work carried out in our institute indicates that there is no deviation from the normal of such inorganic salts as potassium, magnesium, calcium and phosphorus, in a number of dermatoses studied by us. We know that there is an important regulatory mechanism of the body which prevents any of these salts from accumulating to too great a degree in the blood. The determinations mentioned by Dr. Klauder do not vary beyond the latitude of experimental work.

Dr. Klauder's paper is of importance as indicating factors which increase the sensitiveness of the skin to irritants from without.

Dr. Samuel Sweitzer, Minneapolis: I think this paper is of much value to us in regard to the therapy of some of these conditions. I think Dr. Klauder's work will give us a clue to some of the deteriorating changes, and I believe his work on calcium is important. We have been using calcium lactate in urticaria, and his work shows that calcium has something to do with increased irritability.

Dr. Harold N. Cole, Cleveland: I think work of this sort is necessary in an effort to determine whether there is anything that should make us differentiate between eczemas and so-called dermatitis, and it is only by such painstaking and laborious work as Dr. Klauder has done that we will arrive at any definite conclusions. It should be carried further.

Dr. Joseph V. Klauder, Philadelphia: This study is a preliminary report on work that served as a means of orienting ourselves with the problem of studying conditions that increase or decrease sensibility of the skin. It involves many experiments, which could not be incorporated in one paper. For example, a study of the chemistry of the skin and the metabolism of the skin in relation to altered sensibility of the skin, and the influence of certain ductless glands, the thyroid and parathyroid in altering cutaneous sensibility. We are still engaged in this problem.

The study is of particular practical value so far as it concerns the employment of calcium in the treatment of certain skin diseases. I have been administering the calcium chlorid intravenously, which I believe is preferable to the oral administration. I inject from 5 to 10 c.c. of a 5 per cent. solution, biweekly or weekly. It is necessary to inject it very slowly, 1 c.c. per minute. In this way, immediate untoward reactions, consisting notably of a sense of warmth and constriction in the chest, are avoided.

ECZEMA AND DERMATITIS*

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NEW YORK

INTRODUCTION

Probably his contemporaries regarded Cato as a bore, and it is tiresome, no doubt, when a motif is insistently thrummed. Let this be an apology, if one is needed, for again touching on a venerable theme, but one which seems to me never to lose in importance. I refer to the condition called dermatitis by some and eczema by others.

In a given period, at least in private practice, one will see roughly seven cases of eczema or dermatitis to one of psoriasis; eight to one each of pityriasis rosea and urticaria; eighteen to one of lichen planus; nearly two to one each of acne and seborrhea of the scalp; and about eighty to one each of mycosis fungoides, scleroderma, erythema nodosum and dermatitis herpetiformis. Even multiform exudative erythema is encountered only once to thirty instances of eczema, and urticaria pigmentosa once to about seven hundred.

Aschoff's father, himself a physician, is said to have enjoined his son, the German pathologist, to devote his scientific efforts only to problems of practical human significance. Without the least intention of minimizing the worth and fascination of the study of rare diseases, the elder Aschoff's view appeals to me. It seems justifiable to devote not more than a passing thought to the intricate problems connected with mycosis and the exact relation of scleroderma and acrodermatitis to each other, when the equally intricate problems connected with a common disease remain unsolved. Eczema is so common that it is perhaps held in the contempt of familiarity. The patient with scleroderma might be little the worse off if the dermatologist caring for him had not spent five minutes of his scientific life in reflecting on this condition; but the eighty patients with eczema might be infinitely better off if he had devoted five days a month to its common sense study. To dwell on this subject may be regarded as an obsession, as Semmelweiss was supposed to be obsessed by the subject of puerperal sepsis.

This paper will only echo what was expressed by Willan a century ago, and subsequently lost through the magniloquence of Hebra and the resounding rhetoric of Unna. It is hoped that it will contain substantial proof of the identity of eczema and dermatitis. The

* Read at the Forty-Seventh Annual Meeting of the American Dermatological Association, Minneapolis, June, 1924.

question is not so much one of which term should be accepted or rejected in designating the disease, as of the fact that no duality exists.

As Schamberg pointed out in his discussion of this subject in 1923, any inflammation of the skin is a dermatitis, whether it is psoriasis, lichen planus or what not, and the term dermatitis, unless artificially restricted in scope, is thus too general to be used in connection with a definite syndrome. This is fair philologic reasoning, and if the word eczema is regarded as more definitely descriptive, so be it; but we cannot blow hot and cold at the same time. Let the word eczema, then, be conserved with suitable qualifications, but with the reservation that the condition which has been so described is identical with what has also been called dermatitis. If dermatitis is too vague a label for the condition it is supposed to adorn, then so is dermatitis venenata, for in its scaling phases dermatitis venenata lesions may resemble those of psoriasis or lichenification. The expression eczema venenatum might be preferable, but then instead of professional dermatitis we would have to employ the term professional eczema, as the Germans do, and so on down the line. Whatever is decided on, let us cease to befog the issue with etymologic disputes. Let the term eczema be adopted, admitting that it is fanciful, but after all not more ridiculous than any other word. Lichen planus and psoriasis are absurd in themselves, and perhaps the same might be said of table, chair, or any other word apart from the object it connotates. This does not express my own belief, but the concession is offered in order to subordinate a relatively unimportant matter, while we proceed with an analysis of whether, from any point of view whatever, a difference exists between eczema and dermatitis.

The scientific issues to be examined must first be defined. Eczema may be of external or of internal origin. If it is of external origin it could not be produced without predisposition. If it arises internally, it could not be produced without a precipitating external cause. Under neither condition could it be provoked without a local peculiarity of the skin, whether this peculiarity is anatomic, physiologic, functional or produced by previous diseases, conditions or functional states or disturbances of the skin; nor without conditions within the body divisible into similar groups. In exogenic eczema, it is often hard to find the inner predisposing factors. In endogenic eczema, it is often hard to find the precipitating factors. In both, it is often difficult to determine the local peculiarities which make the skin react so as to produce the picture in question. That all of these factors must be present, even if they are not always demonstrable, is the point of this paper; and of this paper the inspiration is axiom one.

Schamberg[1] says: "There can be no doubt that some of these [referring to a group of eczema cases] were not true eczema, but rather forms of chronic dermatitis." Elsewhere[2] he says: "I am afraid that Dr. Highman, in his desire to get away from the use of the term eczema, is setting up another fetish, dermatitis;" and again,[2] "As soon as an eruption of eczematoid character is demonstrated to be due to an external cause, it ceases to be an eczema. I can see no reason for the abolition of the term eczema just because a clinical differentiation may be difficult."

Schamberg, in these three sentences, admits the impracticability of making a clinical distinction between eczema and dermatitis. Therefore, his statement in the first sentence is gratuitous. It is easy to agree with his characterization of the concept of eczema or dermatitis as a fetish, for anything or any concept can be so construed; but when he states that a condition so closely resembling eczema as to be indistinguishable from it ceases to be eczema and becomes dermatitis if its external causation is detected, he admits everything in the argument of this essay. Would he deny that Rome is Rome if he arrived there by the Via Campagna instead of by the Appian Way? Probably not.

Wise[3] asserts:

> Let us imagine that a patient is suspended in a room with nothing about his naked body except the air. If you rub that patient with rhus leaves he will have an attack of dermatitis venenata. For the eruption resulting from contact with poisonous substances, the name dermatitis is still the best designation. Eczematoid eruptions arising from unknown (and presumably internal) causes are best classified as eczemas. If our suspended patient were to get a certain peculiar eruption which we call "eczematoid," without coming into contact with poisonous substances, such an eruption would, in the present state of our knowledge, be designated as "eczema."

This stage setting reflects all of the intellectual inertia retarding our understanding of the problem. In the first place, the subject so exposed to rhus might not develop dermatitis at all. If 100 patients were studied under Wise's conditions, I doubt whether more than forty would develop it. This indicates that the patient, whether because of a general or skin peculiarity, contributes a personal factor necessary to

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1. Schamberg, Jay Frank and Brown, Herman: A Study of the Blood Uric Acid in Diseases of the Skin, with Particular Reference to Eczema and Pruritus, Arch. Dermat. & Syph. **8**:801 (Dec.) 1923.

2. Schamberg, Jay Frank: in discussion of paper by Walter J. Highman: Pathogenesis of Dermatitis, Including Eczema, Arch. Dermat. & Syph. **9**:353 (March) 1924.

3. Wise, Fred: Arch. Dermat. & Syph. **9**:352 (March) 1924.

the production of the disease. In support of this view, the following quotation from a patient's letter may be considered of value:

> Our summer cottage in Michigan is on a tract where poison ivy abounds. Two years ago I contracted a severe case of poison ivy. For fourteen years I had apparently been totally immune. In that time I had pulled up great quantities of ivy, handling it with impunity.

Unless we assume that in 1922 the virulence of the weed in the neighborhood of this man's cottage had increased, we must assume that the man had changed, and this is justified by experience.

If Wise's suspended patient had been exposed to no known external irritant and had nevertheless acquired this mysterious eruption, looking like dermatitis but "eczematoid" (whatever that may mean) in character, and called eczema, it would not by any means prove that no external factors were at fault. Not only admittedly poisonous substances are among the excitants. On the contrary, generally innocuous ones, like guinea-pig hair may be; then why not fine matter of many kinds in the air, unless the subject for experiment is in a vacuum? Why necessarily assume even that a substance working externally is of external origin? It may have originated in the body and have been excreted in the sweat, acting as a local poison, as has been demonstrated to be a possible fact by Bloch.[4] Wise, as well as Schamberg, conceives of only one road to Rome.

At this point, and before proceeding with the argument, I should like to remark: first, that no propaganda is being offered for the abolition of the word eczema; this is stated in order to prevent rhapsodies on the choice of a word. The object of this paper is simple, namely, that irrespective of the word we prefer, we know what we are talking about when we use it. Second, the fact is known to me that many believe, and they always utter their belief with curious unction, that dermatitis of unknown origin is what should be called eczema. This is merely an evasion. If dermatitis is due to a known internal cause it is absolutely one thing: dermatitis of internal origin or eczema of internal origin. If it is due to a known external cause, it is dermatitis of external origin or eczema of external origin. If it is due to an undemonstrable cause, it is dermatitis of unknown origin or eczema of unknown origin. The choice of a name lies with the person, but that the two names mean the same thing is not a matter of choice. It is a matter of fact. This much has been established, at least to the satisfaction of Willan, Bateman, Besnier, Jadassohn, Bruno

4. Bloch, Bruno: Beiträge zur Lehre von Ekzem, Cor.-Bl. f. Schweiz. Aerzte. **39**: 1917.

Bloch, Norman Walker, Engman and Pusey. It is not without timidity that I venture to add what little I can to a doctrine already so ably espoused.

LITERATURE

I shall not recapitulate the older literature, beginning with Willan (1808) and ending nearly a century later with a classical discussion of the subject at the Fourth International Congress in 1900, for this has been reviewed in three articles of mine [5] and references in these, together with the extensive bibliography in Bloch's [6] address at the Congress of the Deutsche Dermatologische Gesellschaft in 1923, will furnish any one interested with the necessary data.

The year 1900, however, marked an epoch in the history of the disease, when Jadassohn expressed his conviction that eczema and dermatitis were identical. This brought the cycle back to Willan, but more particularly to Biette, Cazenave and Schedel,[7] who regarded eczema as a "special reaction of the skin to diverse causes." This belief is fundamental, and was lost until Jadassohn revived it sixty-two years later. Another unheeded echo of the past originated with Walker in Edinburgh, and the chorus has been augmented with increasing vigor in the United States, notably assisted by Pusey and Engman, and somewhat haltingly by others. The present German school is in harmony with this, although it fails to recognize American thought on the subject, for there is nothing fundamental brought out in recent Teutonic writings that has not been advanced in this country and accepted by many Americans for nearly a decade, although Bloch has adduced more corroborative experimental evidence than have we in our country.

Kreibich [8] asserts that:

> Eczema arises only when an internal cause encounters a special condition in the skin. As external causes we characterize substances which come from without or which, through the circulation, reach the outside. As internal causes we group those characteristics which predispose the skin. The reciprocal relation of the two constitutes the etiology of the disease.

The general internal mechanism, according to Kreibich, consists of vasomotor instability, in turn referable to the elaboration of a toxin, as hematoporphyrin in hydroa aestivale; or to a ductless gland

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5. Highman, Walter J.: A Critical Review of Eczema and Dermatitis, J. Cutan. Dis. **34**:259 (April) 1916; Pathology and Pathogenesis of Eczema and Dermatitis, J. A. M. A. **68**:75-79 (June 13) 1917; Pathogenesis of Dermatitis, Including Eczema, Arch. Dermat. & Syph. **9**:343 (March) 1924.

6. Bloch, Bruno: Referate ueber Ekzem, Arch. f. Dermat. u. Syph. **145**:34, 1924.

7. Biette, Cazenave and Schedel: Abrege pratique des mal. de peau. 1838, p. 90.

8. Kreibich, Karl: Referate ueber Ekzem, Arch. f. Dermat. u. Syph. **145**:7, 1924.

or central nervous disturbance causing vasomotor instability. Given a predisposition, many irritants can precipitate the disease. In neurodermite, for example, he found porphyrinogen in one patient. In a woman, whose ovaries had been removed, he produced eczema symmetrically on the ulnar region by applying iodoform plaster on one side only. This indicated the somatic nature of eczema, at least to Kreibich's satisfaction.

Bloch [6] states that:

> The time honored separation of eczemas of outer and inner origin, deeply rooted as it is, and the elimination of "exogenic" eczema from the group under the soubriquet of "dermatitis artificialis" is no longer tenable.

And again:

> Eczema is the interoperation of two factors: the eczematizing agent and the disposition of the skin, without which there can be no eczematization. These two factors are all that is needed to provoke eczema, and the necromantic, impalpable factor denominated "diathesis" need not be sought.

He continues, that clinically, histologically and by all other objective criteria it is impossible to state whether a given case is of external or internal origin, and that "objectively" an eczematized area cannot be distinguished from an area of eczema. Such a distinction is the strategy of embarrassment, resorted to in an attempt to rescue the unfounded "diathetic" hypothesis, and a handicap to the correct conception of the pathogenesis of eczema. He states further:

> There are no metabolic disturbances that can be regarded as characteristic or pathognomic of eczema, and any effort to demonstrate their existence is a hopeless undertaking.

He believes, on the other hand, that "General disturbances and their relationship to and influence on eczema cannot be denied a causative rôle."

Bloch conceives the problem of etiology in eczema as one in which it must be discovered whether there is a special eczematous skin, or whether any skin is eczematous. He favors the former belief, and has used formaldehyd, arnica, mercuric chlorid, iodoform and primrose leaves in his studies, and finds that eczematous skins outnumber non-eczematous ones in the proportion of seven to one. He discounts the use of croton oil as being too violent, essentially a vesicant, and hence not adapted for investigation in this field. He says:

> The requirements for the production of eczema are fulfilled by two factors: eczematogenic irritation, and a receptive skin. Who cannot recall a patient, regarded as a constitutional eczematic, who has not been forced to exist on a diet followed to the accompaniment of arsenic medication, until suddenly, in

a flash of medical intelligence, the truth dawned that the victim was susceptible to primrose or turpentine, whereupon, with the removal of the cause, the "diathesis" vanished?

Predisposition is due, he believes, to allergy and to an infinity of other local causes. He cites the case of Vidal, Abrami and Joltrain, of a man, aged 34, a druggist, susceptible to emetin, whose eczema vanished after immunization. Bloch and Jaeger reported a man, aged 34, with iodin eczema that could be produced by compound solution of iodin and potassium iodid. Administered internally the iodids also provoked the eruption. Likewise, Bloch observed a patient with turpentine dermatitis, one with susceptibility to formaldehyd, in whom hexamethylenamin intravenously administered caused the eruption, and a boy, aged 14, susceptible to quinin, in whom quinin and all its derivatives, as well as leukoplast, caused eczema, although arnica, iodoform, formaldehyd and primrose did not. In this patient, a 1 per cent. solution of quinin instilled into the conjunctival sac caused a local reaction, and when introduced in the nares, asthma. Ten milligrams of quinin hypodermically injected caused a local reaction of dermatitis. In all of these cases, the offending substances produced dermatitis either by local application or when introduced into the body, thus reaching the skin through the circulation. His experiment on the formaldehyd case is not clear, for formaldehyd is derived from hexamethylenamin only in acid mediums, and the body is alkaline. Nevertheless, Bloch is so good an observer that it is difficult to doubt his statement. He concludes that eczema is anaphylactic, anaphylaxis being synonymous with idiosyncrasy in the sense of Doer, rather than of Richet. Bloch says:

Rhus dermatitis according to my point of view, is incorrectly regarded when interpreted as fundamentally different from eczema. The differences in the reaction are quantitative rather than qualitative, and experimental studies by American authors confirm, as do mine with Primula, my belief in the allergic nature of eczema.

He refers to sensitization and desensitization:

To regard eczema as allergic accounts for more of its peculiarities than any other theory.

Riecke, together with Pincus, regards eczema as a:

Clinically and histologically clear-cut reaction of predisposed skin to irritants, whether of internal or external derivation.

He further states:

In a discussion in the dermatologic section of the American Medical Association following a paper of White's on eczema, it was generally held, and with considerable naiveté, that the name eczema should be preserved only for dermatitis of unknown etiology.

After reviewing all phases of the condition, clinical, histologic and etiologic, Riecke [9] asserts that everything supports the "identification of dermatitis with eczema."

Jadassohn,[10] in discussing the symposium outlined in the foregoing, remarked:

> External, and to a lesser extent, internal irritants and idiosyncrasies produce eczema.

And again:

> I have always opposed the differentiation of dermatitis of external origin from eczema, both clinically and microscopically.

Strickler's well-known work proves that ivy poisoning is not a local but an allergic disturbance, and Bivings [11] gives ample corroboration of this fact, as well as of the fact that poison oak dermatitis is also to be so regarded.

Schamberg and Brown,[1] in their studies on the blood uric acid in relation to eczema and other skin diseases, define eczema as an:

> Inflammation of the skin with certain characteristics not due to any external origin.

They quote authorities, such as Tillbury Fox and Garrod, who associated it with gout, and state in their conclusions that excessive uric acid was found in 44 per cent. of their cases of eczema, and that it was strikingly less frequently encountered in psoriasis and other dermatoses, notably, acne rosacea and urticaria. They also point to cures of patients with eczema by regulation of the diet, based on their laboratory findings. In their series of 161 cases they say that some were undoubtedly "not true eczema, but rather forms of chronic dermatitis."

COMMENT ON THE LITERATURE

Precisely eight years ago, I [5] defined eczema as:

> A catarrh of the skin, possessing the pathologic characteristics of an exudative inflammation. It is characterized clinically by redness, swelling, the presence of papules, vesicles, weeping, crusting and scaling in various combinations. In its course it may be acute, subacute, chronic, and its origin depends on an interplay between various known and unknown local and predisposing causes to which the skin lesions are reactions.

In the report on English ivy poisoning [12] I elaborated in detail the probable mechanism underlying the production of eczema. To review

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9. Riecke, Ehrhard: Arch. f. Dermat. u. Syph. **145**:82, 1924.

10. Jadassohn, Joseph: Arch. f. Dermat. u. Syph. **145**:83, 1924.

11. Bivings, F. Lee: Successful Desensitization and Treatment of Poison Ivy and Poison Oak Poisoning, Arch. Dermat. & Syph. **9**:602 (May) 1924.

12. Highman, Walter J.: A Critical Review of Eczema and Dermatitis, J. Cutan. Dis. **34**:259 (April) 1916.

this comprehensively would require too much space, but a few of the more important considerations may be mentioned. The underlying causes include all general metabolic and endocrine derangements and anaphylaxis. The local causes are anatomic, physiologic and allergic or idiosyncratic. The precipitating causes are physical, chemical, parasitic and anaphylotoxic, or substances which act analogously. It is further stated that:

> If the underlying disturbance should be metabolic, substances may be eliminated in the skin secretions whose very presence furnishes irritants capable of acting as precipitating causes on a sensitive skin.

Even without an actual underlying disturbance, the secretions of the skin might be altered in amount or quality so as to act in the same way. This indicates that the skin itself may supply the underlying, local and precipitating factors.

It seems to me that no conclusions were reached in the German symposium that are not expressed in the preceding passages. The paper in question antedates the German meeting, but could not have reached Europe in time to be absorbed into the literature. The unanimity of views expressed on both sides of the Atlantic is the more striking because they obviously originated independently.

Kreibich and Schamberg, respectively, mention disturbances of the ductless glands and nitrogen metabolism as causes of eczema. I can go no farther in agreeing with them than Bloch does when he recognizes such conditions as related factors rather than causative ones. When Bloch recalls the frequency with which a patient, after unavailing restrictions of diet, ordered because of an alleged metabolic disturbance, becomes rid of the eczema on the discovery of primrose excitability, he states a truth within the experience of all. He says: "The diathesis vanishes." It does. One is reminded of how scabies was explained, as eczema still is, by all of the miasmatic hypotheses that rise from the bog of ignorance, until some one found a sensible solution.

Kreibich's belief in vasomotor instability is justified if we regard the affected vessels as among the local causes. We cannot, however, accept without reservation the implications of Schamberg's article on the relation of eczema to an excess of uric acid in the blood. In Schamberg's 161 cases studied, 44 per cent. showed such an excess of uric acid and 56 per cent. did not. It is difficult for me to understand why the 56 per cent. is not the significant figure. It may be unwarranted scepticism, perhaps, but even the test tube, particularly in dermatologic research, seems like an ignis fatuus, if it is leading us back to a belief in the relationship of gout to eczema, a belief last expressed in 1884. Why then, so is psoriasis gouty, and a dozen other dermatoses, and I may be permitted to point out that biochemical research has not

yet, in psoriasis, to which it has been most widely appplied, revealed a single fact important to the patient or to his physician. Reasoning by implication seems to get nowhere; and although a man with eczema may have more than the usual amount of uric acid in his blood, no causal relationship between the two is admissible unless it can be proved first, that in all such instances suitable metabolic treatment cures the disease; secondly, that no external irritant has been operative; and thirdly, that the uric acid itself is not the external irritant in the sense of Bloch, when the blood conveys the substance to the skin with or without the aid of skin secretions.

In this connection, and having been more captivated once by the lure of abstractions than I am now, I examined a great number of patients in general medical wards to see what dermatoses were related to internal disturbances, notably, renal diseases with and without toxic manifestations. I have yet to see a case of eczema in such a patient. This is not entirely conclusive, although it seems significant. It is conceivable that a disturbance of nitrogen metabolism may affect the patient's skin differently when the kidney functions properly than when it does not, or that the basic elements of the disturbance differ under the two sets of conditions.

If Schamberg defines eczema as an "inflammation of the skin, with certain characteristics not due to an external irritant," it is to be regretted that he included in his series cases of chronic dermatitis. His definition would lead to the belief that he commands unique criteria for differentiating the two conditions, and if this is so, he is derelict in not emphasizing them. If such a difference were generally admitted, it would be futile to champion the identity of the two processes. On the other hand, such a difference probably would also have been detected by observers of the caliber of Jadassohn, Bloch, Walker, Besnier, Riecke, Engman and Pusey; and many of these, particularly Jadassohn, have "opposed the differentiation of dermatitis of external origin from eczema both clinically and microscopically." Those who maintain their duality may be the ones Riecke characterizes as showing "considerable naiveté."

Hyperuricacidemia may indicate a predisposition to eczema. Uric acid, reaching the skin from the blood, may be the precipitant of an attack, but it does not seem that more than this can fairly be assumed, or that in all fairness less than this can be allowed, subject to ultimate proof of the fact; but it is neither fair nor sound to assume that a patient with an excess of blood uric acid and eczema has the latter solely because of the former. If he had never had eczema or dermatitis, and became susceptible to primrose or rhus, would the eruption.

under Schamberg's definition, be eczema or dermatitis? In other words, is eczema dermatitis with hyperuricacidemia, or is dermatitis eczema without hyperuricacidemia?

As Bloch says, there are no metabolic processes that can be regarded as "characteristic or pathognomonic of eczema." Bloch's views as to hypersusceptibility seem to point out the one most important, even though not the only, precipitating factor. He defines it as allergic, in no restricted sense, and in my report on English ivy dermatitis his views are paralleled.

> If anaphylaxis and allergy indicate a peculiar response of the organism to alien protein, many nonprotein substances seem to have a similar, if not identical mode of attack, such as primrose.

And again:

> The requirements for the production of eczema are fulfilled by two factors: eczematogenic irritation, and a receptive skin.

My belief is singularly like this:

> . . . an interplay between various known and unknown local and predisposing causes, to which the skin lesions are reactions.

Bloch, in his experiments in the field of clinical study, found ample support for his hypothesis. As already said, he produced eczema both by external application and internal administration of the same toxic substance. His result in the quinin case was strikingly suggestive of anaphylaxis, with the asthma and the conjunctival reaction, and these findings are consistent with what is known of rhus poisoning, sensitization and desensitization.

Inorganic substances certainly act as Bloch reported in the iodin case. Dichloramin-T, applied to the wounded heels of a young officer who came under my observation, would regularly develop a far-flung papular dermatitis within two hours. This would vesiculate and run the typical course of acute dermatitis. In a patient susceptible to mercury, Dr. Goldenberg of New York could produce dermatitis by applying 1 per cent. ammoniated mercury ointment over an area no bigger than the palm. This is not anaphylaxis, perhaps, but no one can deny its close kinship thereto.

The point of Bloch's argument is that in an environment so complex as that of the human being, innumerable causes in susceptible subjects have more to do with the production of eczema than any one other single factor. This is a point of view with which it is easy to agree unequivocally.

A few words as to the identity of eczema and dermatitis, and this analysis will be ended. The modern German school without exception,

Norman Walker in England, Pusey and Engman in this country, support the monistic doctrine. The dualistic doctrine in this country is supported by Schamberg and evidently by Wise. Wise founds his belief on the syndrome of rhus poisoning, an unfortunate choice, since it is precisely rhus dermatitis that is anything but a local condition, according to Strickler, Bivings, Bloch or any one else who has reflected on the facts.

In Japan, so Prof. Charles C. Sleffel, formerly of Columbia University, related to me, children predestined for the lacquer industry used to be exposed to atmospheres impregnated with volatilized lacquer. Those who were apparently resistant were regarded as available, while the susceptible ones were exposed to increased saturations, until they were either desensitized or it was established that they could not be, whereupon they were excluded from the vocation.

Thus there is more to dermatitis venenata than a poison and a person. There is a reciprocal relation between the two. The literature reflects this. The literature also conceives of the cruder general disturbances as contributory, but not immediate factors in the causation of eczema. The trend of recent thought as expressed in the literature, is toward the probability that eczema represents a drama dealing with the microbiology of the cell, in the sense of the latter's exhibiting allergy or a closely related phenomenon, idiosyncrasy, to one or several precipitating factors. These substances reach the skin from without, or if autogenous or incorporated in the body, attain to it from within by means of the circulation or by means of the skin secretions. Once in or on the skin, they behave as though they had appeared there from a purely outside source. If this is so, there is no difference between dermatitis and eczema, and the Europeans have abandoned the term dermatitis.

CASE REPORTS

The first fourteen cases to be mentioned have already been reported in detail,[5] and only an abstract of the findings need be recorded. An ascertainable local irritant caused the outbreak in twelve instances; a hair dye in three, a hair wash in four, resorcin solution in one, a "bust developer" in one, a dye in clothing in one patient and possibly in another, and some vegetable poisoning while doing garden work, in one. Urticaria was associated with the eruption in five patients, and asthma and bronchitis in one. These facts substantiate Bloch's findings as to susceptibility and possible anaphylaxis. Substantiation of his belief in the relationship of general disturbances, not specifically but in a contributory fashion, may be found in this group, for nine of the patients were "nervous," whatever that may mean, ten had mild digestive disturbances, chiefly constipation, and seven had a combination of the

two, all of which signifies, perhaps, only that they lived according to the unwholesome manner of city dwellers. Unfortunately, no biochemical studies were made in this group. However, in support of Schamberg's hypothesis, the average course in patients treated by means of diet and colon irrigation was under nine days, and in those treated only locally, twenty-two days. For this reason, it seems that more importance should be attached to general disturbances than Bloch does, although not quite so much as Schamberg seems to attach to them.

The new cases to be reported will be grouped, so far as feasible, according to the points they purport to illustrate. There are thirteen in all, selected especially to indicate the significant features of the problem, the most significant of which is that whether the precipitating factor is demonstrable or not, the nature of the disease is the same, and the isolation of a determining factor is insufficient alone to warrant differentiation into two groups.

EFFECT OF VEGETABLE POISONS

CASE 1 (Previously reported [5]).—H. L., a woman, aged 22, married, American, a housewife, presented herself on Dec. 3, 1923, suffering with an itching dermatitis on the neck and hands of thirty-six hours' duration. She was subject to ivy poisoning. Her general history was negative. Twenty-four hours before the appearance of the eruption, she had played mah jongg with a new, imported set. She presented the picture of erythematous vesicular dermatitis on the left side of the neck, the eyelids and the right middle finger. On December 4, the hands and forearms were involved. Twenty-four hours later improvement had set in under wet dressings of magnesium sulphate. Percutaneous tests, conventionally controlled and performed on December 4, with pulverized shavings from the ivory of the tiles, bamboo of the tiles, ivory of the counters, lacquer from the trays and from the case, gave positive results with the last two, which were distinctly more papular, painful and tender a day later. The papules lasted two days longer. The other tests and controls were negative. Lacquer shavings applied to the unbroken skin after the manner of Markley, on December 7, produced vesicular dermatitis in forty-eight hours. On April 22, she had a fur dermatitis of the neck, giving positive percutaneous tests after the technic of Markley.

Summary.—This is a case of lacquer dermatitis in a patient susceptible to ivy poisoning and to certain furs. The sensitivity to lacquer and fur were experimentally corroborated. This is an example of Bloch's polyvalent sensitization.

CASE 2.—M. S., a woman, aged 20, married, American, a housewife, is the sister of the previous patient. She presented herself on Dec. 3, 1923. She had been similarly exposed and at the same time as her sister, to lacquer. A rash appeared on the left side of her neck within thirty-six hours. Tests as in Case 1 produced the same results but of less intensity, and without persistent papulation. She gave no history of rhus poisoning.

Summary.—This is a case of lacquer dermatitis and the patient was monovalent.

Case 3.—M. L., a girl, aged 20 months, the daughter of the first patient, presented herself on Oct. 10, 1923. She had a vesiculopapular eruption of the buttocks and groins and lichenification of the right elbow flexure. The general history was negative.

Summary.—This case is mentioned as a probable example of the familial eczematic tendency of the French. "Il n'ya pas l'eczema, il n'y a que des eczematiques."

Case 4.—J. R., a woman, aged 22, married, American, housewife, who presented herself on March 26, 1924, had an eruption that appeared regularly after playing mah jongg with any one of several sets. Thirteen months prior to the first visit, she developed vesicular dermatitis from the use of sulphur ointment. Another ointment, the ingredients of which were not known to her, caused erythema and scaling of the hands. Lobsters and crabs caused urticaria. She had vernal and autumnal asthma (spring grass and rag weed). Her blood pressure was low after a confinement. On March 26, she had vesicular dermatitis of the hands. Tests, as in Case 1, gave positive results. She now washes in alcohol after playing mah jongg, and there have been no recurrences, even when she has handled sets formerly toxic.

Summary.—The patient belonged to the polyvalent eczematic type of Bloch (lacquer, sulphur and other substances) and was sensitized in a profounder way as well (rose and hay-fever). She also had a tendency to low blood pressure.

Case 5.—R. T., a man, unmarried, American, of Italian extraction, a florist, who presented himself on Jan. 31, 1924, had a history of an itching eruption of the eyelids of two months' duration. In May, 1923, he had been similarly affected. His general history was negative. The eyelids were swollen, red and scaling, but the conjunctivae were not involved. There were a few desquamating patches on the chin and cheeks, and a red, vesicular disk, as large as a quarter, on the flexor side of the right wrist. The facial condition resembled the so-called "seborrheal dermatitis" or "eczema," the condition on the wrist looking like chronic vesicular eczema. His occupation warranted the suspicion of plant poisoning, and primroses had been placed in stock shortly before the onset of the disease.

Extracts of various flowers and plants being handled were made in the following way: The leaves, stems, petals, stamens with pistils and ovaries were separately steeped in 95 per cent. grain alcohol for five days. This was filtered, and the filtrate itself was used for some tests, and for others, the residue, evaporated at room temperature and redissolved in decinormal sodium hydrate and conventionally controlled. The percutaneous method was followed. No difference was noted in the results of the two procedures. Thus on February 11, tests were performed with *convalaria majalis* (lily of the valley), *primula obconica, primula malacoides* and galax. The last is a leaf used in floral decorations. The galax and leaves of both varieties of primrose gave strong reactions, as did the galax and primrose stems. The blossoms of *primula obconica* also gave positive reactions which persisted as small papules for thirty-six hours.

On Feb. 12, 1924, lacquer from some Japanese flower baskets handled by the patient was applied as in the mah jongg cases, with negative results. On March 18, he was again tested against galax, with the original findings, and against the stems and petals of iris, with negative results. On February 16 and 21, further tests were made by directly applying to the skin the crushed

leaves and stems of suspected plants, the test substances being held in place by moist gauze under adhesive tape, and the skin having been previously made slightly red by ten minute exposure to hot water applications. In ten hours, erythema appeared at these sites, which vesiculated in forty-eight hours. Controls with moist gauze applied as in the foregoing were negative. On February 13, petals of *primula obconica* were rubbed on the eyelids, which began to smart twenty-four hours later, and which were swollen and red next day. On March 18, 1923, the patient, by avoiding contact with the offending agents, had been free from any eruption. At about this time, he was preparing for the flower show, and was exposed to primroses. His eyelids became swollen. A similar exposure provoked a recurrence on the face and hands. Since then, by dint of sponging his hands and face with 80 per cent. alcohol, he has been free from the eruption.

Summary.—This patient had a polyvalent susceptibility, proved by his history and tests. Clinically, he had what is popularly known as "seborrheal dermatitis."

Case 6.—The patient suffered from English ivy poisoning, and as it has already formed the basis of an earlier article,[12] the details of this history have been recorded. Only the salient features will be restated. For a year, he had been suffering with an eruption called chronic eczema by one authority, seborrheal dermatitis by another, and dermatitis venenata by a third. His face, arms and neck were involved when he first presented himself on Dec. 15, 1922, and the picture was that of scaling, lichenified, crusted and weeping eczema at the enumerated sites. At times his arms, shoulders and back were affected. He was sensitive to rhus and had studiously avoided it. He handled English ivy (hedera helix) a great deal. He responded percutaneously to this plant, and has been free of this disease since April, 1923. He is also susceptible to sunlight, which causes dermatitis starting as sunburn, and terminating in a residual disc shaped hyperpigmentation about 1 inch (2.5 cm.) in diameter, and less sharply circumscribed than fixed erythemas, on the left side of the forehead. He has marked seborrhea. Extensive metabolic studies revealed no abnormalities.

Summary.—This patient is an example of polyvalent sensitization (rhus and hedera). He has an unstable vasomotor system in the sense of Kreibich, shown by the dermatitis solare. There are no ascertainable metabolic disturbances. Munro's case, quoted by Prosser White, showed persistent susceptibility. In the patient discussed this seems to be true as well, for percutaneous tests are still positive.

EFFECT OF FUNGI

In these two cases, the etiologic explanation has been based on probabilities, for bacterial investigations were not made. Some of the lesions, or rather some of the sites affected, were so strikingly suggestive that the clinical asumption seemed warranted, and in one instance subsequent events substantiated the hypothesis.

Case 7.—B. R., a youth, aged 18, a student, a native of Georgia, had suffered since infancy with a red eruption of the face and body. Between the ages of 13 and 15 this disappeared spontaneously, only to recur with greater intensity, but now confined to his body. The itching was severe, particularly at night. On Sept. 17, 1923, when he first presented himself, his torso, the flexor aspects more than the extensors of his limbs, the hands, to some extent the perineum,

scrotum and the interdigital spaces of the feet, as well as the soles, were covered with a variegated eruption. This consisted of vesicular, scaling patches of lichenification, weeping and crusting, together with excoriations. His condition had been regarded by a prominent dermatologist, holding a university chair, as chronic eczema. The examinations he had conducted were all negative. Thus his nitrogen and carbohydrate metabolism, test meals, stool examinations, studies in basal metabolism, the glucose and phenolsulphonephthalein tests, urinalyses and protein sensitization tests, as well as physical examination, showed nothing abnormal. The lesions on his feet and perineum suggested those seen in dermatophytosis. The other lesions did not. Whitfield's ointment was prescribed. In two days, there was a marked improvement, and in four days rapid involution of the eruption was obvious. This would mean little in itself in support of the presumptive etiology, were it not for the fact that his father, who had accompanied him on his trip north, had developed an eruption which he showed me on the last day the boy was examined. This was a typical small patch of epidermophytia inguinale in the right groin. The father, who had never had a skin affection before, had slept with his son on the trip. The boy has been well for eight months.

Summary.—This is an example of eczema in a person without a solitary ascertainable metabolic or physical derangement, and caused by a fungus. The father's infection, reminiscent of Koch's requirements, indicates this far more trenchantly than anything else could. That it was clinically eczema is unquestionable, or the diagnosis of one of our ablest colleagues would have to be disputed.

Case 8.—H. M., a man, aged 62, American, a physician, who presented himself on May 24, 1920, had an eruption that had begun on his back seven months previously, and which had spread elsewhere two months later. From his neck to his toes, and including the body folds, he was covered with all the types and combinations of lesions and their sequelae that it is within the versatility of eczema to produce. He was weak, almost tottered when he walked, and was harried with incessant itching. His legs and feet were markedly edematous, although the urine was negative and the heart functioning properly and without murmurs. One group of physicians had incriminated proteid foods, another carbohydrates. In spite of being a physician himself, he had eliminated both classes of sustenance from his diet with uncritical credulity, and for three months had subsisted on nourishment so meager and characterless that it might have enervated even an orchid. The lesions on his feet and in his groins suggested those of dermatophytosis. Whitfield's cream was prescribed. In a week he was improving and the marantic man was gradually guided back to an adult human food intake. The edema began to diminish. Certain local indications were met with tars and the roentgen ray. In a month he was well, and the eruption has never returned. The original clinical diagnosis was confirmed by an eminent New York dermatologist, who also concurred in the etiologic hypothesis.

Summary.—This is a case of eczema of "metabolic origin" in which the patient was cured by salicylic and benzoic acid used externally.

EFFECT OF METABOLIC DISTURBANCES

Case 9.—F. O., a woman, aged 51, American, a dressmaker, who presented herself on Oct. 9, 1923, had an eruption that had afflicted her for six months. It began as a vesicular rash, and disappeared without treatment after two months, only to return with greater severity, involving the face and the flexor

surfaces of the limbs. She gave a history of gastroptosis and mucous colitis followed by constipation. The face, hands, cubital fossae, neck, chest and flexor surfaces of the forearms were covered with vesiculosquamous, weeping, lichenified eczema. With various fluctuations, this eruption had come and gone. It disappeared completely after four weeks, and returned ten days later, disappearing again after a month and remaining away for two months. On March 11, 1924, it recurred, and since then has been extremely obstinate. On the whole, coal tar salve gives most relief. Suprarenal gland extract has been used internally, but apparently with little effect. The most exhaustive laboratory examinations as to the alimentary tract, urine and blood chemistry are negative. She has visceroptosis. Protein sensitization tests are negative. Nothing in her environment or habits seems to explain the origin of her malady.

Summary.—The patient had chronic, recurring eczema without any ascertainable cause, internal or external.

CASE 10.—S. S., a woman, aged 64, German-American, a housewife, who presented herself Sept. 19, 1921, had a vague history of an eruption that had occurred at varying intervals for seven years, with swelling of the eyes, neck and tongue, stiffness of the legs and drowsiness. She had myxedema. Under thyroid therapy, she began to improve, when suddenly, after two weeks of treatment, she developed a follicular vesiculation of the eyelids and neighboring regions of the face. This responded rapidly to soothing lotions. Two months later, a similar eruption appeared on the ears and nares, and two months after this on the eyelids and face. In March, 1923, the hands also became involved. These outbreaks would run a transitory course under wet dressings, and appeared to be related to thyroid ingestion. From October, 1923, until recently, the entire torso was covered with the eruption. Symptomatically, the myxedema is controllable with great precision, but the skin always remains dry. A year and a half ago she was placed on thyroxin, 2 mg. twice a day, and during the ensuing year was almost free from the eruption. This supported the belief that byproducts in the other thyroid preparations were the cause of the eczema, a hypothesis which became untenable with the recurrence of the eruption last winter. In September, 1921, a general physical and laboratory investigation showed the following findings, only the significant ones of which will be noted: low basal metabolism (rate 32 per cent. below normal); blood sugar and blood nitrogen negative (uric acid 3.75 mg. per hundred cubic centimeters); cholesterol, 252 mg. per hundred cubic centimeters (high); hemoglobin, 45 per cent.; red blood cells, 3,552,000; differential and leukocyte counts normal; slight poikilocytosis and anisocytosis (aplastic anemia); renal function, normal; urine, negative; occult blood in stools (hemorrhoids). On May 12, 1924, colon irrigations were ordered. The first irrigation intensified the itching. Subsequent ones have not done this, but the eruption is worse than it has ever been.

Summary.—A patient with myxedema, low basal metabolism, high cholesterinemia, secondary anemia, has eczema of the face, hands, arms and torso, which is worse in winter. No external cause could be ascertained, unless it were the effect of cold weather on the dry skin of the patient.

MISCELLANEOUS CASES

CASE 11.—H. W., a girl, aged 14, American, a student, who presented herself on Feb. 3, 1923, had an itching eruption of two months' duration on the scalp, neck and chest. The lesions on the neck and chest were papulovesicular and erythematous, with scaling patches, lichenified over the right clavicle and nape

of the neck. The entire scalp was covered with a dense, gray, scaling eruption extending beyond the hair line to the forehead. On removing the scales, an exuding surface was uncovered. There was no marked falling of the hair, and no fungi were found in the hair or scales. Treatment with roentgen rays and by other conventional applications produced varying degrees of improvement of varying duration. On two occasions, in March, 1924, she went swimming in an indoor pool, and the eruption on her neck and face grew more severe, her eyes smarted, and her lids grew red. Her general history was negative. Inquiry as to the disinfection of the swimming pool elicited the report that a drop of chlorin a minute is introduced, the capacity of the pool being 70,000 gallons. No disinfectant is used for the towels.

Summary.—A healthy, adolescent girl has obstinate eczema of the scalp, face and neck. All investigations are fruitless. An infinitesimal concentration of chlorin in the water of a swimming pool irritates the eruption. Whatever the cause of the original outbreak, she is also susceptible to a known inorganic chemical, and thus is probably an example of Bloch's polyvalent eczematic type of person.

CASE 12.—E. P. S., a woman, aged 42, American, a housewife, who presented herself on Nov. 9, 1923, had an eruption of two weeks' duration involving the entire body, but restricted on the mentioned date, to the neck, chest, shoulders and eyelids. She had had hay-fever for two summers, and had been placed on a low protein diet because of constipation. At the sites before mentioned, she had an erythematous, papulovesicular rash. This responded within a week to wet dressings and lotions. Eighteen days later, a sudden recurrence appeared, after playing mah jongg with a set she had obtained just prior to the first outbreak. She gave positive percutaneous tests as in Case 1, but there seemed to be other elements involved. Subsequent recurrence took place without exposure to lacquer. On Nov. 15, 1923, the blood sugar was 0.11 per cent. and the blood uric acid 3.4 mg. per hundred cubic centimeters. The stool was highly acid. Colonic irrigations, later suggested, were of no benefit to the eruption. On Dec. 12, 1923, she consulted another dermatologist, and finally was cured under various kinds of local treatment. No explanation of the etiology was furnished.

Summary.—This is a type of eczematic skin in a person subject to hay-fever. The patient is probably in Bloch's polyvalent group. With the exception of the acid stools, no general disturbance could be found. The amount of blood uric acid was not increased.

CASE 13.—J. S., a woman, aged 27, American, a trained nurse, who presented herself on April 25, 1924, had "dermatitis venenata" of the face, neck, chest, shoulder and right thigh. The eruption itched intensely. There had been no exposure to rhus or primrose. On May 3, she was well. On May 17, there was a recurrence after an application of face cream. The ears and neck were involved, and twelve hours later the cubital fossae, to which no application had been made. A percutaneous test was positive.

Summary.—In this case there was susceptibility to some ingredient in a massage cream, with an eruption at the site of application and elsewhere, showing Kreibich's somatic affection of unexposed sites.

ANALYSIS OF CASES

The general impressions of eczema reflected in this paper are derived from a series of 718 cases, of which 125 are instances of so-called

dermatitis venenata and occupational dermatitis; 176 clinically in the dermatophytosis group; five in diabetic patients, and thirteen which are seasonal in nature. This leaves 396 unclassified cases. Since it is only during the last two years that the quest for the precipitating cause has been more or less intensively followed, it is safe to venture the statement that this large group of unexplained cases would have been appreciably cut down had they been more actutely studied, for in the thirteen recent cases only four failed to yield a solution.

In the old series of fourteen cases, precipitating causes were found in twelve and a digestive disturbance in ten. In the new series of the thirteen cases, a single precipitating cause was found in four (Cases 2, 7, 8 and 13); several precipitants in six (Cases 1, 4, 5, 6, 11 and 12, lacquer, ivory and fur in Case 1; lacquer and sulphur in Case 4; primrose and galax in Case 5; rhus and English ivy in Case 6; an undemonstrated cause and chlorin in Case 11; and lacquer and an undemonstrated cause in Case 12). No precipitant, or one and at least another undiscovered one were found in four (Cases 3, 9, 10 and 11). In Case 6, sunlight also seemed to be a factor. In Case 7 and probably in Case 9, fungi appeared to be excitant.

From the standpoint of precipitants, the exciting factors may be tabulated as follows: physical causes, one case (Case 6, sun); inorganic substances, three cases (Case 4, sulphur; Case 11, chlorin; Case 12, massage cream); vegetable substances, seven cases (Cases 1, 2, 3, 4, 5, 6 and 12); fungi in two cases (Case 7 and probably Case 9); and animal substances in one case (Case 1).

Of the general disturbances found in patients who also had eczema, these facts, positive and negative, may be set forth: Anemia was present in Case 10, in the patient with myxedema. Alimentary disturbances were found in three patients (Case 9, visceroptosis; Case 10, increased itching after colon irrigation; Case 12, acid stools); hypothyroidism with decreased basal metabolism in Case 10; disturbed carbohydrate metabolism was looked for and not found in Cases 9 and 10, and in Cases 9, 10 and 12 no disturbance of nitrogen metabolism, with special reference to hyperuricacidemia was ascertained. Cholesterinemia was present in Case 10. General evidence of anaphylaxis was found in Cases 4 and 12 (hay-fever) and somatic affection in Case 13. No general disturbances could be discovered in these thirteen cases. On the other hand, it must be recalled that in the original series, studied, from the standpoint of the effect of general therapy on the course of the disease, the patients receiving colon irrigations ran a much shorter course than those who did not.

THE NATURE OF ECZEMA

Eczema and dermatitis may be identical or not. One may be due solely to internal disturbances, the other solely to external. If both are due to the same influences, an admitted probability, the diseases are identical.

This is a list, doubtless incomplete, of internal causes to which eczema has been ascribed: the dartrous diathesis of the French, the gouty diathesis of the English, the exudative diathesis of Czerny, and in modern times these have respectively been dressed up as the unknown cause: hyperuricacidemia and the lymphatic inflammation of Szamberger. Further hypotheses include colitis, constipation, intestinal fermentation, intestinal indigestion, foodstuffs, starch ingestion, disturbed fat, carbohydrate and nitrogen metabolism, changes referable to the menopause, autointoxication, renal dysfunction, disturbances of the sympathetic system, trophoneuroses and endocrine dysfunction. No further commentary is needed on the lack of significance of this ample, one might call it collect, other than to let its amplitude speak for itself; but it might be pointed out that generically the same views were held about scabies, until the acarus was discovered, whereupon a whole literature spectrally vanished.

It is undeniable that eczema has an underlying cause, imperative that this cause be sought, and desirable that it be found, but it is questionable whether the foregoing list includes the direct underlying cause. The direct underlying cause, together with its remoter subsidiary factors, is whatever renders the skin susceptible to a precipitating agent. Here we must agree with Bloch that the mechanism is likely to be closely allied to, if not identical with, anaphylaxis. Unfortunately, anaphylaxis, broadly interpreted and not confined to protein sensitization, reduces itself to idiosyncrasy or susceptibility, and the last term would seem to satisfy the requirements of the problem.

The quest for the internal factor, or better, the unknown factor in the production of eczema, as of other dermatoses, has set apart a group of investigators who have been styled "internists." They regard all cutaneous manifestations not obviously neoplasms, anomalies, infections or the result of external agents, as the result of internal agents. They ally dermatoses to internal medicine, and to view cutaneous diseases from this standpoint, when done critically, shows proper enlightenment. It would show even more enlightenment, however, to avoid a partisan attitude, and to try to determine when the point of view of internism, in its narrow sense, is inapplicable. It would appear fair to expect of internism the ability to recognize just as clearly when it is not dealing with a disease of primarily internal origin as when it is. The demands of logic would be better served. To peruse the pages on eczema in the

"Practical Medicine Series of 1923 on Dermatology" is to discern how vague the work is that connects eczema with general disturbances.

It seems to me that failure at this point is more a question of ignorance of methods than anything else. As a practical matter, any general disturbance in a patient with eczema must be considered and should be treated, for its more or less immediate relationship to the disease cannot be denied, but its direct relationship has no foundation in fact or experience.

Leavng aside the vaguer diatheses, which are meaningless concepts and masks for ignorance, let us examine some of the conditions meriting more serious thought. Disturbed carbohydrate metabolism is present in some people who have eczema. In a few diabetic patients, eczema is encountered. A connection between the two cannot be denied, but how rarely it is found! In the present series of 718 cases, it was encountered only five times. The striking fact is that the vast majority of eczematic patients have not diabetes or any allied disturbance, and the vast majority of persons with such disturbances have not eczema. Nevertheless, when the two coexist, and the skin improves under general treatment, the causal relationship is strongly substantiated.

Hyperuricacidemia was found in 44 per cent. of Schamberg's cases of eczema. In the few patients I have studied with this point in mind, the figures were normal. Ignoring this, however, the conspicuous thing in Schamberg's series seems to me to be that 56 per cent. of his patients had normal blood nitrogen coefficients. For the rest, the same line of reasoning applies as outlined in the preceding paragraph. Furthermore, I have yet to see a chronic nephritic patient with eczema, and it would be reasonable to expect to find eczema in nephritic subjects at least as often as in nonnephritic subjects, if nitrogen chemistry disturbances had much to do with the matter.

And so too with cholesterinemia, alimentary disturbances, endocrine disturbances, anemia and the rest. Nevertheless, occasionally patients respond to general treatment, especially to colonic irrigations. The explanation seems to lie in the fact that there are several grosser internal disturbances, and particularly those connected with abnormal chemical substances in the body, presenting a relationhip to eczema that may even be the main factors in its production. A clue as to how they work may be found in the relationship of hematoporphyrin to hydroa aestivale. We are looking for the greatest common divisor. Even in hydroa more is needed than hematoporphyrin, namely, the sunlight; nor does sunlight without hematoporphyrin cause hydroa. The two factors, the underlying one and the precipitating one, are required, to say nothing of a third, a peculiarity of the affected tissue. So too must it be with eczema. But eczema is not a specific disease, as typhoid fever is, or as

impetigo contagiosa. A great many substances and conditions provoke it. It is a reaction, as urticaria is a reaction.

The underlying causes are unquestionably manifold and are latent or active, according to the presence or absence of a reciprocal irritating cause. Roughly speaking, something suggesting receptors must be in the cells affected, so as to produce eczema when these cells are exposed to a definite substance or substances or condition of affairs. Such cellular receptivity may be indicated, or even enhanced by general diseases or disturbances, but these diseases are not in themselves the cause. The causes will probably be found in some as yet only lightly tilled field of biology. They have to do with immunity, and eczema is due to the breaking down of the resistance of the skin.

As the body's envelop, the skin should be able to resist the countless onslaughts from without, chemical, physical and parasitic; and the countless attacks by substances engendered within, which may be in solution in the skin secretions or present in the cutaneous circulation; but the skin cannot always successfully accomplish this. It must have a threshold of resistance, determined by the anatomic, as well as the biologic character of the cells. When this threshold is overstepped, subject to the nature of the anatomic reaction of the tissue to the given agent, a more or less characteristic, morbid picture is produced. Next to erythema, the least specialized of the cutaneous responses, come wheals and simple inflammatory exudation. Eczema, pathologically, is such an exudation, and the more generic the response, the greater is the number of agents capable of provoking it. The underlying mechanism, however, may safely be assumed to be constant.

Extraneous factors are pathogenic in a manner not difficult to understand. Their pathogenicity depends on their concentration, virulence or intensity, according to whether they are chemical, parasitic or physical agents. Nor can they operate unless the skin is vulnerable, and vulnerability is a local variable further modified by the health or disease of the body as a whole. If this were not so, the skin would always be diseased.

As Bloch has shown, substances capable of producing eczema when applied locally may also do so when introduced into the body, reaching the skin primarily by means of the circulation, and secondarily in solution in the secretions. Having so reached the skin, the mechanism by which they produce disease is identical with that determining their pathogenicity if externally applied. It is probable that some simpler known autogenous substances are actually locally toxic. Perhaps uric acid may be one, but it is more likely to be some whose existence is not yet even suspected. If manufactured internally, when they reach the skin by the routes mentioned, they become precipitating causes. This establishes the identity of eczema or dermatitis of external with that of

internal origin. The difference between the two is merely a matter of how the excitant reaches the skin. By whichever avenue, there is no distinction in the end results either clinically or anatomically, although there may be a difference in the course, for it is obviously easier to discover and limit the activity of an extraneous than of an internal agent. The presumptive internal agent may act alone as the precipitant, or in conjunction with one or more external agents, and the converse is equally probable. This determines the matter of monovalence or polyvalence of the cutaneous response. The final factor of importance is the susceptibility of the attacked cells, which may be referable to the phenomenon of allergy or mere idiosyncrasy, or due to other congenital or acquired biologic or anatomic characteristics.

It may be argued, and with considerable justice, that the thesis of this paper supports nothing newer than the doctrine that eczema indicates a simple tissue peculiarity. It would be futile to try to deny this, or to clothe the fact in those figurative phrases with which ignorance attires itself; but if the thesis is as stated, it may also be said that efforts at explaining eczema as a manifestation solely of a general disturbance are confusing, because they are profoundly untrue. Every attempted explanation along these lines has fallen far short of its object, while the search for the precipitating factors is constantly justifying itself more and more by accretion of evidence. Cases of eczema in which a precipitating factor, usually external, cannot be found, are diminishing in number, and when I am unable to find such a factor in a given patient, I always have a distinct sense of personal failure. Without losing sight of the possibility of an internal toxin, whether introduced from without or engendered within the body, I am reluctant to comfort myself with the evasion that the cause cannot be found, for it is more likely that my own limitations are to blame.

At this writing, the patient with myxedema (Case 10), who also has anemia and cholesteremia, and whose eruption was never so severe as when she was taking colon irrigations, is getting better since all treatment based on the general findings has been abandoned, and since Lassar's paste and starch baths are being used. The patient (Case 7) with dermatophytosis presented a distinct picture of eczema, and all general treatment failed, but he became well under suitable local applications. Cases due to parasites seem to follow the ordinary laws of susceptibility and resistance, and often illustrate them nicely. Frequently, they give a history of having had restricted patches of the disease for a number of months or years, and of then being suddenly attacked by the widely disseminated process. This bears out all of the clinical, allergic and immunologic observations in the domain of phytology recorded by Bloch, Plato, Jadassohn, Kaufmann-Wolf and others.

Allergy in its restricted sense explains little regarding eczema, for protein sensitization, at least so far as its influence can be determined in eczema, plays an inconspicuous rôle. A broader use of the term, in which it would be synonymous with idiosyncrasy, perhaps, would explain not only the cases due to protein sensitization, but to all other substances. Years ago, in discussing a group of papers on anaphylaxis in urticaria, Pusey remarked, at a meeting of the Section on Dermatology of the American Medical Association, that he could see no distinction between idiosyncrasy and anaphylaxis, except that the former was the term of greater content, the latter a restricted explanation of one aspect of idiosyncrasy. He jibed me at the time for my fundamentalism. Today it is apparent that Pusey's view was that of common sense. That same common sense would behold in the explanation of eczema as tissue idiosyncrasy enough scientific value at least to avoid the error of charging the disease solely to the account of internal causes, which explain so much that they explain nothing.

The internal causes, as already stated, must either be substances in themselves pathogenic to the skin when they reach it from within, or capable of breaking down the skin's resistance to external causes. In either event, the ultimate action on the skin is that of a precipitating agent. These internal agents must be numerous. Whether disturbances in body chemistry, recognizable by known laboratory methods, are indexes of the presence of the unknown agents, cannot be denied or affirmed. Certainly nothing so simple as hyperuricacidemia itself can be the cause of eczema. In hyperuricacidemia the other tissues, undoubtedly including the skin, contain as much uric acid as the blood does. If uric acid under these conditions produced eczema, it seems to me the fact could be demonstrated; and I believe I have experimental evidence, which will be published in due time, indicating that this substance is not eczematogenic, whatever its remoter relationship may be to this disease. There is also evidence, which will be reported later, indicating that the peculiar susceptibility in question lies in a field so far little studied.

In short, eczema is the result of a skin idiosyncrasy to precipitating causes, external in a preponderance of instances and internal in the remainder. The external causes include organic and inorganic substances, parasites and certain physical agents, notably actinic rays. Their working mechanism is explained by the phenomenon of allergy or a similar process. To act, they require a susceptible skin. This susceptibility is local in the skin, and the result of congenital or acquired conditions in that tissue. If acquired, they may be due to alterations incidental to growth and age or previous local or general disease. General disease presupposes inner alterations, underlying causes in fact,

so modifying the body, including the skin, that the skin loses its resistance to previously harmless agents. In a sense, this is one with the group of local causes. The local and general disturbances are effective through lowering the threshold of skin resistance to precipitating causes whatever their source.

CONCLUSIONS

Eczema is an exudative cutaneous inflammation due to the effect of pathogenic agents precipitating a morbid response in prepared tissue. Understanding this will stimulate inquiry as to the nature of the preparation of the skin and as to the nature of the precipitants. It will also identify two processes still too widely considered separate, namely, dermatitis and eczema. It will satisfy the requirements of both the so-called internists and externists, eliminating dualism and promoting the only rational philosophy that can be brought to bear on the theme, that of the monists. It will increase the burden of those who seek to explain the disease as an internal disturbance by maintaining, as evidence of their belief, findings that always fall short of proof. It is not an external disease or an internal disease. It is both, always, and at one and the same time.

To be a good internist in dermatology, and nothing is more admirable than a good one, it is important to know when not to be an internist. The alimentary, urinary and several other tracts; the endocrine, nervous and several other systems; the biochemical changes in the body, have been explored in vain for the source of eczema. It is encouraging, when studies of this sort have failed, to find that after all the enigma can be solved by finding out that the patient is susceptible to rhus, lacquer, primrose, galax, English ivy, mercury, sulphur or perhaps a pathogenic fungus, and that he can continue to have too much uric acid or cholesterin in his blood, or always have acid stools, and still be cured of eczema. In like manner, he can have the eczema and have none of the disturbances mentioned. It is discouraging not to find the precipitating offender, but with care such disappointments can be reduced in number. In any event, the point of view in question is simple and direct, and has the advantage of being without pedantry or extravagance, and of conforming to the few definite facts that are known.

As to the name for the disease, always a theme for great emotional display, and the least important consideration in the matter, Riecke's declaration may well be heeded, that we Americans show peculiar naiveté in differentiating between eczema and dermatitis. There is no difference, and to say that dermatitis should be the term employed when the cause of the disease is known, and eczema when it is unknown, is merely a jingle. It has not even the philosophic background of a political campaign slogan, than which nothing is emptier. Since the

term eczema is so firmly intrenched, and against all reason, perhaps it would be better not to make its use the point of attack, even though "simple dermatitis" describes the disease histologically, and identifies it clinically. The main issue is to understand the nature of the disease.

The practical question that remains after everything else has been debated, is how to approach a case of eczema with reference to the relief of the patient. There can be no valid objection to appraising his disease from all clinical and laboratory aspects and treating him accordingly; but this is not treating his skin affection. The outstanding requirement here is to discover its cause, and this can best be accomplished by exercising ingenuity and originality. It can be done six times out of seven, and will usually be found to be something amazingly simple. If this is done, there will be fewer instances like the one in which the patient with dermatophytosis was rendered marantic, because, on conflicting medical advice, he attempted to eschew both protein and carbohydrates at the same time. Nor will there be a case like the one of dermatophytosis, which persisted all the time that a growing boy, needing proper food, was restricted in his diet because of the mandate of certain laboratory findings which proved meaningless. Nor will there be many cases such as the one of myxedema, in which the postponement of the use of Lassar's paste put off the patient's ultimate improvement, while the unhearing deity of hypothyroidism was being worshipped. In other words, to regard eczema simply, as internists of course, but as internists knowing their own limitations, will tend to keep eczema off the Island of Laputa, where nothing scientific belongs.

DISCUSSION

Dr. Richard L. Sutton, Kansas City, Mo.: I congratulate Dr. Highman on his scholarly and highly scientific dissertation.

I believe that in a considerable percentage of cases anaphylaxis is an important etiologic factor in eczema. While it is difficult to unearth the offending protein in many instances, considerable help usually can be derived by the use of skin tests, and in suspicious cases, we have made such tests a routine procedure in my office.

Dr. J. Frank Schamberg, Philadelphia: Since Dr. Highman does not wish to abolish the use of the term "eczema," I think our divergent attitudes are matters of phraseology rather than of conception. I agree that an inflammation of the skin, or eczema due to some internal cause, and an inflammation of the skin or dermatitis of external origin, cannot always be differentiated histopathologically or clinically. I agree perfectly to that, but what concerns me in this matter is the use of such terminology as may confuse our mental attitude toward these classes of cases. Those who are localists in their tendencies are looking for local causes, and those who believe the cutaneous disturbance in question is due to systemic origin are making detailed examinations for internal causes; therein to me lies the danger of the blind acceptance of one attitude or the other. It appears to me that we have to combine our comprehension of etiologic factors in such a manner as to evaluate each properly.

I will not deny that external irritation may be a factor in many cases of so-called eczema, provided that Dr. Highman includes such slight influences as friction of clothing, external heat, excessive perspiration, etc. I am not prepared to say that we may not have an eczematous eruption due solely to poisons generated within the body. I think there are many internal disturbances that definitely bring about skin eruptions.

Dr. Highman said that he made a survey of a large number of patients in a hospital, who were suffering from renal and other diseases, and he could not pick out a single patient with eczema. To my mind that is not astonishing. I have gone through institutions for the tuberculous and have examined 600 patients without seeing a single case of lupus vulgaris. Lupus vulgaris is rare among the tuberculous, but visceral tuberculosis is common in lupus patients. I think the same arguments may, in a way, be applied to eczema. Eczema may be rare among the nephritic subjects but varying grades of renal disturbance may be common in eczema. I believe that in patients above the age of 50 defective renal elimination is a prominent factor in the causation of pruritus and eczema. I am quite sure that intestinal toxemia is a frequent cause of eczema.

I had a patient whom I had treated for a long time for obstinate eczema. I finally came to the conclusion that there was a strong probability of the trouble being due to intestinal toxins. After much persuasion, the patient consented to consult a gastro-enterologist, who, after colonic irrigations and other treatment, promptly cleared up the condition. Now when she has a recurrence, she very properly goes to the gastro-enterologist instead of coming to me. I think that this is the crux of the situation. We have to determine in each individual case which is the dominant factor. We know that of the many exposed to ivy poisoning, only one in a number is susceptible. Even in such cases, while the ivy poison produces the dermatitis, some other factor influences susceptibility, but the rhus toxin is the dominant etiologic factor.

We must endeavor to study our patients thoroughly, and try to develop an increased clinical acumen to the end that we may better recognize the chief causative factor in any given case of eczema or dermatitis.

Dr. Augustus Ravogli, Cincinnati: In my opinion, the older I grow the less I believe that eczema is an entity in itself. I believe it is a synergic phenomenon. We have an eczema and a dermatitis that may come from a scratch, but between the two I find the same difference that occurs in simple coryza and rhinitis. There is the presence of some element that changes the dermatitis into an eczema. Eczema may come from internal conditions, but so far no antibodies have ever been found in eczema, but probably porphyrin which is laid on the skin sensitizes the skin and is the cause of the dermatitis and of eczema.

As to uric acid in the blood, I do not know whether we will be able to produce eczema in that way. Like any acidosis, it produces an urticaria, and probably because of the scratching, eczema may be produced. Probably because of the acidity in the blood, the lack of calcium causes the capillaries to become permeable, and the serum of the blood passes into the tissues and so produces the condition which we find in eczema, but I do not believe that eczema is a pathologic entity in itself, but only an epiphenomenon.

Dr. Walter J. Highman: It seems as though the Schuylkill and the Hudson were flowing in a common channel. I agree with Dr. Schamberg when he says that it is neither an external nor an internal disease. In my paper, I make the statement that it is both always and both at the same time.

As Dr. Schamberg has pointed out, I think the difficulty is in finding the dominant factor. A patient may have all the underlying causes enumerated, but unless some toxin is generated that goes to the skin, the patient will have the internal irritation without the skin reaction, and without the underlying factor that makes the patient susceptible, external factors will be harmless. If something of this sort were not true, we should always have this, that or the other skin disease; the skin would fail entirely as a protecting envelop.

Curiously enough, although in the first series of cases colonic irrigation definitely shortened the course of the disease by 60 per cent., in the patient with myxedema in whom I thought the colonic irrigations might be of some use the eruption flared up. Immediately after the first irrigation, she complained of itching, and we had to abandon the colonic irrigations. In another patient with eczema of about a year's duration, with visceroptosis and other diseases, the alimentary tract being negative otherwise, a day or two ago I found that she had acquired a cat about the same time that developed the eczema, and that the cat slept on her bed. I made a percutaneous test with the cat's hair, and she responded. However, the eczema is rapidly disappearing since she has stayed away from the cat. That patient had underlying disturbances which could not be recognized.

I think Dr. Schamberg is right in saying that we cannot by any supersense determine the dominant factor, but that the question is one of determining the dominant factor in every case. The external factors are the easier to find.

I hope I did not give Dr. Sutton the idea that I thought the food tests had anything to do with eczema. I am not talking of sensitization in the sense of Richet at all, but in Dore's sense, which is tantamount to saying idiosyncrasy, which is tantamount to saying nothing.

CACTUS SPINE PSEUDOTUBERCLE

REPORT OF A CASE ASSOCIATED WITH LUPUS VULGARIS, PULMONARY AND LARYNGEAL TUBERCULOSIS *

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Pseudotubercles, due to the introduction of foreign material into the skin are of especial interest to dermatologists, not because the tumors themselves carry a serious prognosis, but because so often they are mistaken for the more serious granulomas and neoplasms.

True tumor formation in the skin found pathologically to be foreign body tubercles has followed the subcutaneous introduction of paraffin, liquid petrolatum and camphor oil.

REVIEW OF THE LITERATURE

As early as 1906, Heidingsfeld [1] made an extensive microscopic study of the changes resulting from subcutaneous injection of paraffin. This author states that:

> The distinguishing and characteristic pathologic changes are the Swiss-cheese-like general appearance under the low powers of the microscope, the alveolar-like distribution of the inflammatory products and the abundance of giant cells. . . . The reaction resembles in its general appearance a granuloma, much like that of an early acute tuberculosis before caseation takes place.

In more recent years, reports have been made of many foreign body tumors having as their etiologic factors the mineral oils. Essentially, these tumors are alike both clinically and histologically. They are insidious in their onset, developing from a few weeks to a year following injection, relatively asymptomatic, rarely degenerating or undergoing necrosis, having a tendency to form daughter tumors along the adjacent lymphatics, and to recur following surgical removal. Histologically, they resemble the well-known paraffinomas occurring following the injection of paraffin in cosmetic surgery.

Among the first to describe mineral oil tumors of this type are Jacob and Faure Fremiet,[2] who report cases following the injection of

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* Studies and contributions from the Department of Dermatology and Syphilology of the University of Michigan, service of Dr. Udo J. Wile.

1. Heidingsfeld, M. F.: Histopathology of Paraffin Prosthesis, J. Cutan. Dis. **24**:513, 1906; A Further Contribution to the Histopathology of Paraffin Prosthesis, J. A. M. A. **51**:2028 (Dec. 12) 1908.

2. Fremiet, Jacob, and Fremiet, Fauré: Rev. de chir., 1917, Nos. 9 and 10, p. 221-262 (Sept.-Oct.) 1917.

camphor oil in liquid petrolatum. In one of the six cases of camphor oil tumors observed by Mook and Wander,[3] a laboratory diagnosis of tuberculosis was returned.

Why certain persons react by tumor formation to the subcutaneous introduction of foreign body material, is still unknown. Individual predisposition has been suggested as a possibility. In discussing the three cases studied by Letulle and Alglave,[4] Balzar states that he observed tumors following the injection of liquid petrolatum occurring in patients with tuberculosis, evidently believing this to be a predisposing factor. This is interesting, because the patient under our care had definite cutaneous and pulmonary tuberculosis in addition to the foreign body pseudotuberculosis.

The clinical resemblance of pseudotubercles to true tuberculosis is emphasized by DuBois,[5] whose patient developed nodosities following the injection of camphor oil into the arm five months before.

In a case reported by Bivona,[6] a young Italian had received intrascrotal injections of liquid petrolatum, the procedure resulting in the development of a paraffinoma. This tumor was at first thought to be a gumma.

Sounding a warning note that careful differential diagnosis should be made between foreign body tumors, tuberculosis and neoplasm, Stokes and Scholl[7] report a case of tumor caused by liquid petrolatum, developing in the arm of a soldier, following an injection during typhoid fever eighteen months before. In this case, a pathologic diagnosis of tuberculosis was returned.

From the experimental side, van Gelderin,[8] in 1921, produced paraffinomas in a dog by subcutaneous injections of paraffin. More recently, Weidman and Jefferies[9] proved experimentally in monkeys that the subcutaneous and intramuscular injections of paraffin oil are capable of producing granulomatous tumors, histologically resembling paraffinomas. These tumors developed as soon as three and as late as eleven months following injection. They proved also that liquid petrolatum and not camphor oil was the causative factor. They ruled out the possibility that tuberculosis may have been a predisposing factor by making

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3. Mook, W. H., and Wander, W. G.: Camphor Oil Tumors, Arch. Dermat. & Syph. **1**:304-318 (March) 1920.

4. Letulle and Alglave: Bull. de l'Acad. de méd., Paris, **84**:9 (July 6) 1920.

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9. Weidman, F. D., and Jefferies, M. S.: Experimental Production of Paraffin Oil Tumors, Arch. Dermat. & Syph. **7**:209-222 (Feb.) 1923.

a definite statement that at necropsy neither animal was found to be tuberculous. Here, as in other instances,[10] individual predisposition is stressed as playing a rôle in the occurrence of these tumors, and Weidman [11] states that:

> Certain individuals have a tendency to react unduly against formed foreign bodies in general, by the familiar tissue proliferation in which giant cells are so conspicuous, in a way that other individuals do not. So that, provided the individual's tissues are thus disposed, the foreign body reaction will take place regardless of whether the foreign body is hard paraffin, soft paraffin, liquid petrolatum, celloidin or cellulose.

The use of mineral oils as vehicles for drugs injected into the skin is condemned by him.

Occasionally, the vegetable oils may give rise to tumor formation, as indicated by Sutton's [12] patient, who developed subcutaneous nodules following the sixth injection of mercury salicylate suspended in linseed oil.

During the influenza epidemics from 1919 to 1921, camphor oil injections were used freely. In some instances, the mineral oils were used as excipients, instead of the vegetable oils. Large quantities of this combination were shipped for use in foreign countries.

There is under our observation at the present time, a patient who spent two years in Russia. While he was in Poland, he developed typhus fever. For this illness, he received fifteen subcutaneous injections of camphor oil incorporated in a mineral oil, in each arm. Two years following these injections, he noticed small nodules in the upper right arm. Examination at the present time reveals three split pea to cherry size, hard, noninflammatory, rather deeply seated tumors on the extensor surface of the upper right arm. There are no associated symptoms. His past history is negative, except for an attack of tuberculous pleurisy in 1919. Undoubtedly, these tumors are paraffinomas, although as yet no biopsy has been made.

In addition to the pseudotubercles described, there is evidence that other foreign bodies may provide similar reactions.

Warthin [13] reports a case of cactus spine pesudotuberculosis in a nurse, who, while on a visit to New Mexico, brought back to her home many species of cacti. She sought advice for a nodular eruption occur-

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10. Weidman, F. D.: Camphorated Oil Tumors, J. A. M. A. **78**:58 (Jan. 7) 1922.

11. Weidman, F. D.: The Danger of Liquid Petrolatum in Parenteral Injections, J. A. M. A. **80**:1761 (June 16) 1923.

12. Sutton, Irwin C.: Tumor Formation After Injection of Mercuric Salicylate in Vegetable Oil, Arch. Dermat. & Syph. **7**:223 (Feb.) 1923.

13. Warthin, A. S., and Davis, J. E.: Cactus Spine Pseudotubercles, Ann. Clin. Med. **2**:248 (Jan.) 1924.

ring on the forearms and thighs. These nodules were only slightly painful and seemed to be definitely associated with the lymphatics. This condition had been diagnosed previously, by various observers, as lupus vulgaris, syphilis and neoplasm. Microscopically, the nodules consisted of pseudotubercles conglomerated into longitudinal masses, and made up of epithelioid cells, foreign body giant cells, fibroblasts, plasma cells and lymphocytes but no caseation. In the giant cell masses which characterize most of the pseudotubercles, foreign body material was strikingly evident. The true nature of the foreign body was suspected, and the fine hairlike spines and coarser prickles of the cactus plant were embedded, cut and stained. Microscopically, the pathologic picture here was identical with that of the foreign bodies found in the cutaneous lesions. The patient disposed of the cactus plants, and the eruption disappeared in three months.

In the same article, mention is made of a tuberculous patient, who, on returning from California, presented an eruption of similar nature, suggesting lupus vulgaris or blastomycosis, and even histologically diagnosed coccidioidal granuloma by one pathologist, who mistook cross sections of the cactus bristle for the organism of this condition. The case reported below is also mentioned. Warthin makes the interesting observation that biopsy material sent to him from a number of such cases, with the exception of the case reported by him, came from persons with definite or suspected pulmonary phthisis. In addition, there was cited a case of a boy who developed a large indurated mass in the parotid region, which was diagnosed and operated on as a tuberculous lymph node. On pathologic examination, it was found to be a pseudotuberculous mass encapsulating a large rose thorn. In conclusion, Warthin stresses the similarity of cactus spine pseudotubercles to the granulomas and neoplasms.

Of special interest, however, is the patient recently under our care. In this patient, in association with true pulmonary phthisis, laryngeal tuberculosis and lupus vulgaris, there occurred lesions resembling cutaneous tuberculosis and blastomycosis, which, however, proved to be cactus spine foreign body tubercles.

REPORT OF CASE

History.—M. G., a man, aged 25, entered the University Hospital, July 17, 1923, for examination of lesions behind the left ear and over the right mandible, accompanied by weakness and hoarseness. His mother, five brothers and three sisters were living and well. There was a history of pulmonary tuberculosis in the father. There was no history of cancer. The patient had had the usual diseases of childhood, with recovery. Beginning the latter part of 1918, after his discharge from the army, the patient developed a persistent cough and night sweats. In January, 1919, he was examined by his physician, who told him that he had tuberculosis, for which treatment in an army hospital in Arizona was immediately begun. For the past five months, hoarseness had been

a troublesome symptom. During the past month he had noticed pain in the chest and rapidly progressing weakness.

In November, 1921, two months after leaving Arizona, while in Los Angeles, he noticed a small split pea-sized "growth" over the right mandible. This lesion was irregular in outline, covered with a fine scale and noticeably pruritic. He said that there were many cacti in Arizona, but he did not remember ever having come in contact with them. In June, 1922, similar lesions appeared in the scalp and over the right shoulder. These lesions were diagnosed and treated as lupus vulgaris, in a Chicago hospital. By December of the same year, eight such lesions were noticed scattered over the back, chest and legs. His condition at this time was diagnosed by a physician in

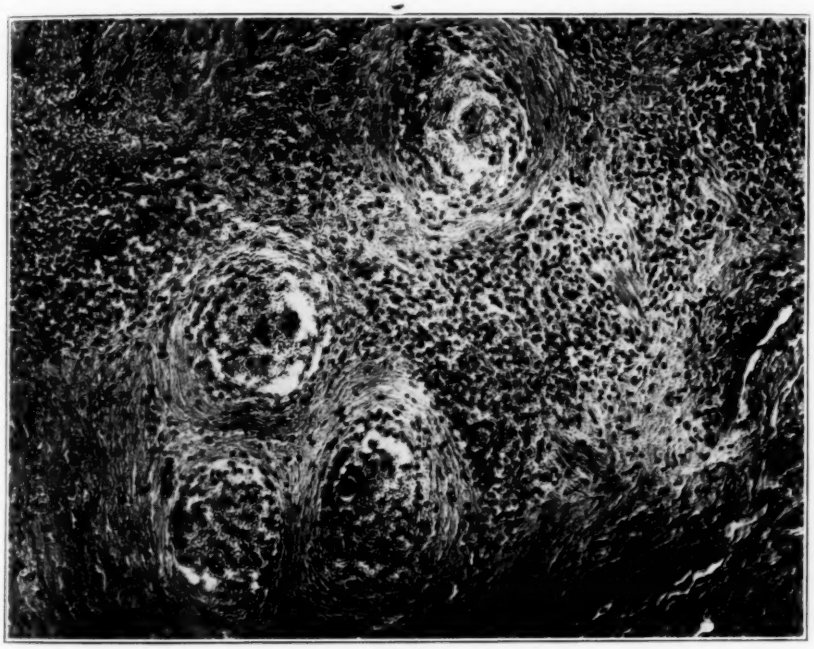

Fig. 1.—Low power magnification view of cactus spine pseudotubercles. The cactus spines are in various states of disintegration.

another Chicago hospital as blastomycosis, and several lesions were excised and treated subsequently with ultraviolet light, with decided benefit. Nine months before presentation, the present lesion over the left mastoid appeared.

Physical Examination.—The patient was a rather poorly nourished young man with a sallow color and a hoarse voice. He presented two lesions, one over the middle third of the right side of the mandible, and the other in the left mastoid region. The lesion over the mandible was irregular in outline, approximately 1½ inches (3 cm.) long and three-fourths inch (1.57 cm.) wide. The lesion presented a dull erythema and some scaling. In the border were many glass pinhead to small pea-sized nodules, which were yellowish brown under the diascope. The center of this lesion showed an atrophic scar. There was some associated telangiectases present, evidently the result of roentgen-ray

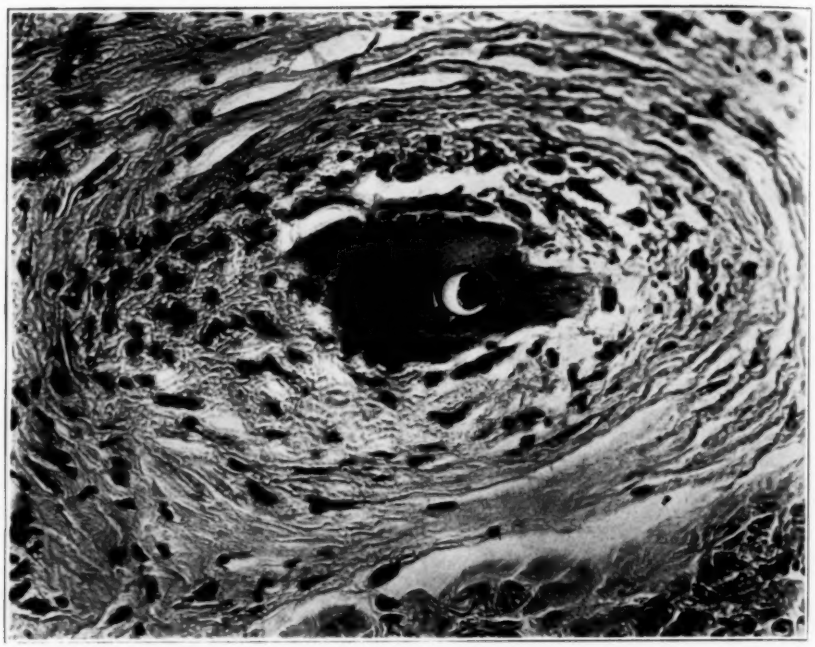

Fig. 2.—High power magnification of a cactus spine in the center of a foreign body giant cell.

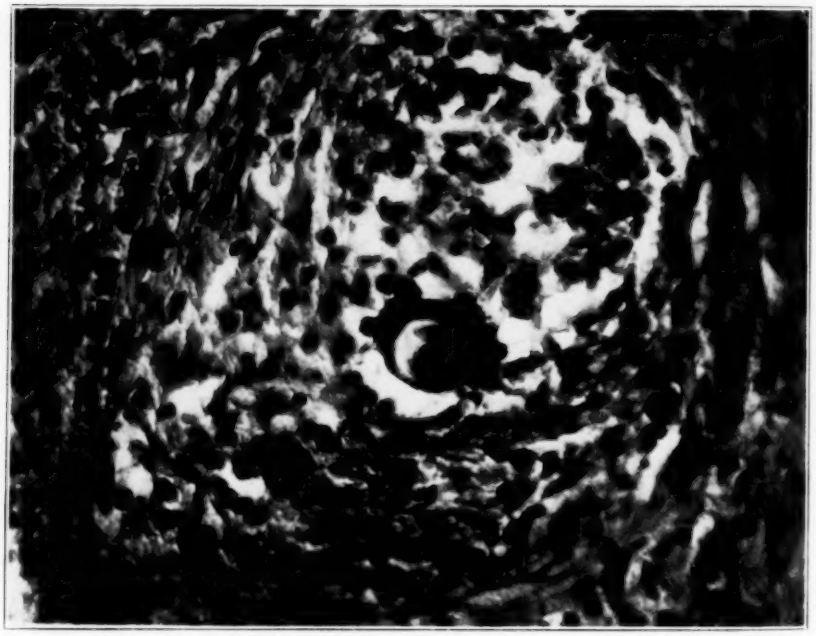

Fig. 3.—Cross section of a cactus spine in the center of a foreign body tubercle.

treatment. The lesion over the left mastoid bone was more active and more circular in outline, being approximately the size of a silver dollar. It was fairly sharply circumscribed, and the border was definitely raised above the level of the surrounding skin for about three-fourths inch (1.57 cm.) This lesion was brightly erythematous and showed considerable scaling and crusting. This lesion showed, over its entire surface, but more marked at the border, a number of pinhead-sized pustules. To palpation, the lesion was moderately infiltrated but practically painless. Clinically, it had a slight resemblance to blastomycosis. In the larynx, there was a large ulcerative lesion involving the left side; the base was necrotic and covered with secretions. This lesion had the appearance of an infective granuloma, probably tuberculosis. The mucous membranes of the mouth and nose were negative.

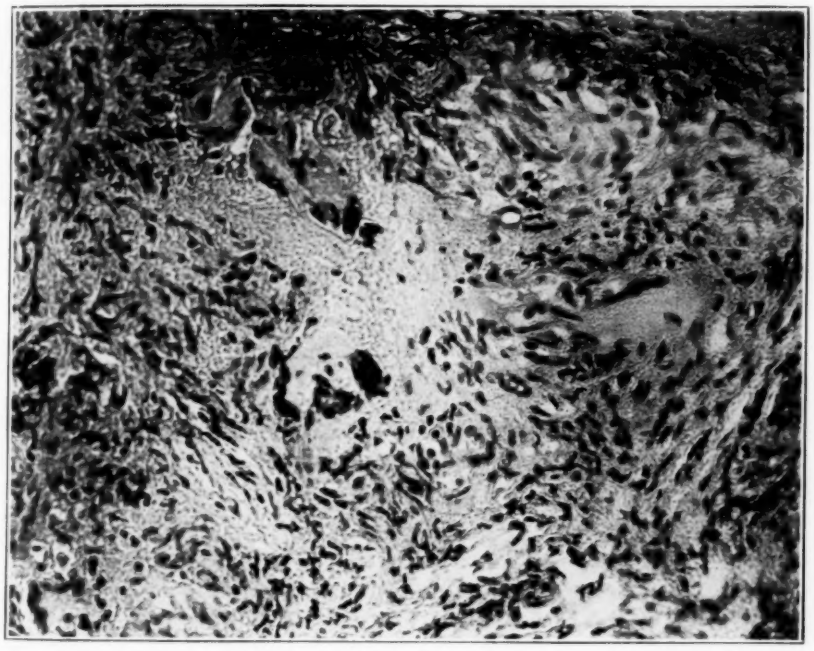

Fig. 4.—Biopsy taken from larynx, showing miliary tubercles.

Examination of the chest showed dulness over the entire left side of the chest and upper half of the right side, with increased spoken and whispered voice sounds. In addition there were many râles scattered over the entire chest. Roentgen-ray examination substantiated the clinical findings, showing undoubted evidence of an active pulmonary tuberculosis.

Biopsy.—(This report was received from the Department of Pathology, University of Michigan.) Biopsies were performed on the lesion back of the left mastoid, on the lesion over the right mandible and on the larynx. Biopsy taken from the lesion over the left mastoid showed thickening of the horny layer and slight hyperplasia of the interpapillary cords of the epidermis. The papillary layer and the corium showed fibrosis, with numerous areas of lymphocyte and plasma cell infiltration. Scattered through the corium, particularly in the upper portion were numerous foreign body pseudotubercles (Fig. 1).

These were well encapsulated with a whorl of dense connective tissue and were made up of fibroblasts and foreign body giant cells. In the latter were foreign bodies that on cross section showed a central hyaline core staining deep pink, and in other cases staining bluish, as if becoming calcified. Around this core, often attached to it, but frequently separated by a contraction space, there was a dense, hyaline, pink staining cortex. Neither the core nor the cortex was translucent, and there was no double refraction on change of focus. These were much larger than blastomycetes and did not show the doubly refractive capsule of the latter organism. They showed no nuclear matter in the deep staining central core.

Further longitudinal and oblique sections showed that these foreign bodies were elongated. They corresponded in appearance and staining properties to the fine tips of cactus hairs, and comparison to the latter showed identity of appearances. The pseudotubercles were elongated, extending along the long axis of these hairs. The latter showed varying stages of disintegration and digestion by the foreign body giant cells. There was no caseation of these pseudotubercles and no well developed epithelioid cell formation as in the true tubercle. They showed various stages of healing, the foreign body giant cells splitting up into fibroblasts, and eventually the formation of a fibroid scar, showing a definite encapsulation and concentric arrangement of fibers of coarse hyaline connective tissue.

Biopsy taken from the lesion similiar to lupus over the right mandible showed a combination of two processes, the first of which was made up of a group of true tubercles composed of avascular epitheloid tissue with few giant cells, with peripherally arranged nuclei. The centers of these tubercles showed early caseation. This group of miliary tubercles presented the appearance of a lupus lesion. In the same section, there was one large pseudotubercle, consisting of encapsulated concentric fibrolastic tissue, in the center of which there was an enormous foreign body giant cell showing irregular processes and containing in its center a cactus hair (Fig. 2). One foreign body pseudotubercle due to a cactus hair occurred in a lupus lesion (Fig. 3).

Biopsy from the vocal cord (Fig. 4) consisted of a mass of conglomerated miliary tubercles, in various stages of development, the majority showing more or less advanced caseation. No pseudotubercles were found and no foreign body inclusions. The majority of the tubercles were caseating, epithelioid miliary tubercles, without giant cells; others contained characteristic giant cells of tuberculosis. This lesion was purely tuberculous.

Summary of Pathologic Condition.—The first biopsy showed a pure pseudotuberculosis due to fine cactus spines without any true tuberculosis. The second biopsy from the face showed a typical lupus lesion containing one cactus spine pseudotubercle. It was impossible to include these two processes in the same photomicrograph, owing to the fact that they were so far removed from each other. The third biopsy from the larynx showed a pure active miliary tuberculosis. Hence, the case was one of pseudotuberculosis due to cactus spines, associated with true lupus vulgaris, laryngeal and pulmonary tuberculosis.

ACNITIS, WITH PARTICULAR REFERENCE TO THE BACTERIOLOGIC FINDINGS

REPORT OF A CASE *

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AND
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We report the results of the study of a case of acnitis, with a detailed account of animal inoculations and cultural bacteriologic findings.

Smears made from the purulent exudate from an open lesion revealed the presence of staphylococci and a gram-negative bacillus. It is interesting to note that these same findings were reported to us by a laboratory in another city where smears had been examined some months earlier.

REPORT OF CASE

Miss S. K., aged 20, consulted us Oct. 3, 1923, with an eruption on the face of four months' duration. She was a nurse in a hospital, and she feared that from accidental contact with some patient she had possibly acquired a syphilitic infection.

About June 1, the patient developed some reddish macular spots on the chin. These slowly increased in size, and new lesions appeared. Subjective symptoms were absent. The patient did not observe any departure from health so far as her well-being was concerned. She had been treated with ultraviolet light and vaccines without any effect. A Wassermann test had been made, which gave a negative reaction. The eruption consisted of about three score lesions on the chin and a dozen outlying efflorescences on the cheeks and forehead. The lesions consisted in the main of pinhead to millet seed sized, reddish papules and nodules having a glistening or waxy looking surface. On the cheek were several pea-sized lesions, which were obviously deeper and involved the hypoderm. Two or three of the papules were breaking down and suppurating. Several weeks later, a crop of new lesions appeared on the forehead and upper part of the face. Some of these lesions had their origin in the hypoderm and first exhibited the appearance of subcutaneous nodules. The overlying skin became reddened as the nodules acquired elevation and prominence. The lesions terminated with suppuration and healed, leaving oval, round or irregular pitted and excavated scars.

On Oct. 31, 1923, the face was improving. A comparison of photographs with the actual condition on the face indicated a partial involution of the lesions on the chin. By March 1, 1924, the lesions had undergone complete involution, leaving disfiguring scarring.

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* From the Research Institute of Cutaneous Medicine.

* Read at the Forty-Seventh Annual Meeting of the American Dermatological Association, Minneapolis, June, 1924.

On October 3, a lentil seed sized, nonulcerated nodule was removed from the skin over the right lower maxilla. The skin was cleansed with 95 per cent. alcohol and painted with tincture of iodin. This was permitted to dry and was then removed with alcohol. With a Keyes skin punch the lesion was removed, the punch excising a button of skin down to the subcutaneous tissue. Under strictly aseptic conditions, the specimen was divided into two parts—one for histologic and pathologic study, and the other for bacteriologic study and animal inoculations.

Histologic Examinatiion of Nodule from Patient.—The histopathology of acnitis is fairly uniform and the description need not be set forth in great detail; the picture is briefly portrayed in order to confirm the clinical diagnosis. The epidermis was virtually normal. Under low power magnification the entire corium from the subpapillary layer to the subcutaneous tissue was the

Fig. 1.—Acnitis; author's patient.

seat of a dense and diffuse cell infiltration. The cells were chiefly of the lymphoid type, but numerous areas exhibited large numbers of polymorphonuclear cells. In these localities, there was considerable fragmentation of the nuclei. Grouped in areas of the midcorium were clusters of giant and epithelioid cells. There were half a dozen giant cells in a single field. The cells varied greatly in size and shape. Some of the nuclei were arranged in horseshoe or annular configuration, while others were grouped irregularly. The giant cells contained from three to a dozen nuclei. The center of the cell took the eosin stain well. Some of the giant cells were apparently thrombosed vessels. There was throughout the section marked dilatation of the blood vessels and lymph spaces. There was no circumscription of the inflammatory process to the sebaceous or sweat glands; all of the elements of the cutaneous architecture were invaded. The sections were stained for acid-fast bacteria and for other organisms, but the examination was entirely negative.

Bacteriologic Study.—The part of the section of skin reserved for bacteriologic study was emulsified in a sterile mortar in a small amount of 0.1 per cent.

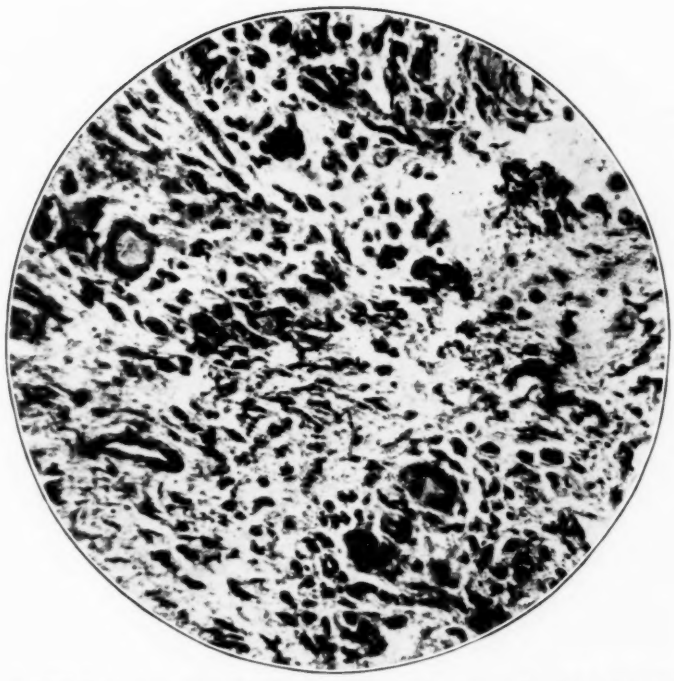

Fig. 2.—High power magnification of skin lesion in author's patient, showing giant cells.

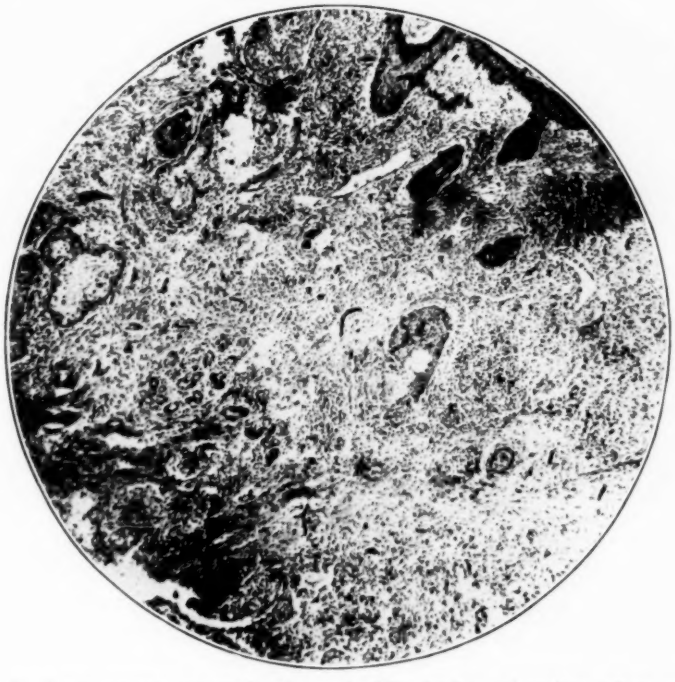

Fig. 3.—Low power magnification of skin lesion, showing giant cells.

glucose hormone broth. Microscopic examination of this broth suspension, stained with Loeffler's alkaline methylene blue, Gram stain and for acid-fast organisms, did not reveal anything.

All cultures were made in hormone broth, plus 0.1 per cent. glucose and brain tissue, p_H 7.2. They were incubated aerobically and anaerobically at 37.5 C.

Aerobic Cultures.—Cultures in the brain medium when incubated for seven days showed ring formation at the surface of the bouillon and considerable turbidity, with a small amount of flocculent sediment. Microscopic examination of the culture stained with Gram stain revealed: (*a*) many cocci, moderate in size, single and in various sized bunches, which were gram-positive; (*b*) many smaller cocci, arranged in tetrads or fours, showing a capsule; these were separate tetrads and groups of tetrads; all were gram-positive.

Blood hormone agar plates showed the following colonies:

Colony 1 (twenty-four hours): This was a moderate sized colony, round, with smooth surface, convex, edge entire, white, opaque and caused no hemolysis or change in the blood agar medium. Microscopically this was a moderate sized coccus, single and grouped in various sized bunches; it was gram-positive.

Colony 2 (twenty-four hours): This was a small colony, round, with a smooth surface, convex, edge entire, gray-white to translucent, somewhat moist, with no change or hemolysis of the blood agar medium. Microscopically, there was a small coccus arranged in tetrads or fours; there was evidence of a capsule in some groups, while in others it was absent; it was gram-positive.

These colonies were picked out and streaked on hormone blood agar slants and incubated at 37.5 C. for twenty-four hours, when they appeared as follows:

Culture of Colony 1: Hormone blood agar slants showed abundant, filiform growth along the line of inoculation. The growth was raised, glistening, smooth, white, opaque and somewhat viscid; the medium was not changed. On microscopic examination of slant agar, a moderate sized coccus, single and grouped in various sized bunches, was found to be gram-positive. It was identified as *Staphylococcus albus.*

Culture of Colony 2: Hormone blood agar slants showed a scanty, filiform growth, raised, glistening, smooth grayish white, of a somewhat slimy consistency; the medium was not changed. Microscopic examination on slant agar revealed a small coccus, in tetrads or fours, grouped in various numbers of fours, which was gram-positive. It was identified as *Micrococcus tetragenous.*

Anaerobic Cultures.—The anaerobic cultures in a brain medium broth were incubated for seven days and showed a ring formation at the surface of the bouillon, marked turbidity and an abundant flocculent sediment. Microscopic examination of the anaerobic culture stained with gram stain revealed: (*a*) many cocci, of moderate size, single and in bunches, which were gram-positive; (*b*) many smaller cocci, arranged in tetrads or fours, single tetrads and groups of tetrads, which were gram-positive; (*c*) small rod, the dimensions of which were: length, from 2.5 to 4 microns; width, from 0.5 to 0.8 microns; some larger forms were observed; they appeared single and in pairs end to end, with rounded ends, evenly stained, with no spores and gram-negative.

Blood hormone agar plates showed the following colonies:

Colony 1: This was of moderate size, round, with a smooth surface, convex, edge entire, white, opaque, and caused no hemolysis or change in the medium. A microscopic examination revealed a moderate sized coccus, single and grouped, which was gram-positive.

Colony 2: This was a small colony, round, with a smooth surface, convex, edge entire, gray-white to translucent, somewhat moist, with no change or hemolysis of blood agar medium. A microscopic examination revealed a small coccus, arranged in tetrads or fours, single tetrads and groups of tetrads, which was gram-positive.

Colony 3: This was of moderate size, round, with a smooth surface, convex, edge entire, yellowish-gray to translucent, somewhat moist with no hemolysis or change in blood agar medium. Microscopic examination revealed a small rod, the dimensions of which were: length, from 2.5 to 4 microns: width, from 0.5 to 0.8 microns, more or less uniform in size; which appeared single but occasionally in pairs end to end, rounded ends, evenly stained, no spores, no capsules, and was gram-negative. These colonies were isolated from the blood agar plates and streaked on hormone blood agar slants.

Culture of Colony 1: The colony was abundant, filiform, growth raised, glistening, smooth, white, opaque, somewhat viscid; the medium was not changed. Microscopic examination revealed a moderate sized coccus, single and grouped in various sized bunches, which was gram-positive and was identified as *Staphylococcus albus.*

Culture of Colony 2: This was a scanty, filiform growth, raised, glistening, smooth, grayish-white of somewhat shiny consistency; the medium was not changed. Microscopic examination revealed a small coccus in tetrads or fours, grouped in various numbers of fours, which was gram-positive and was identified as *Micrococcus tetragenous.*

Culture of Colony 3: This was a moderate growth, filiform, raised glistening, smooth, translucent, no pigment, with slight musty odor, of viscid consistency; the medium was not changed; there was no hemolysis. Microscopic examination revealed a small rod, the dimensions of which were: length, from 2.5 to 4 microns; width, from 0.5 to 0.8 microns; some larger forms were observed; they were mostly single, with rounded ends, no spores, evenly stained, and were gram-negative. Subcultures of the cultures were also made in hormone broth, plus 0.2 per cent. glucose incubated at 37.5 C., giving an abundant growth, with ring formation, even turbidity, and heavy flocculent sediment. In microscopic examination of hormone broth subcultures, the organism appeared as a somewhat larger rod, single but also in twos and threes end to end, ends rounded. Bipolar staining was also observed. When transplanted to hormone blood agar or plain hormone agar the organism again appeared smaller and lost the bipolar staining. It remained gram-negative on both mediums. As this organism was present in the anaerobic cultures of the skin emulsion and not in the aerobic cultures, a further study of its biologic characteristics was made, which revealed: motility, active; cultures in litmus milk: one day, acid; three days, acid; seven days, acid; no coagulation; gelatin, at 37.5 C., no liquefaction; Russell's double sugar medium, butt, AG; slant, acid; indol, negative; nitrates, reduced to nitrites; Voges-Proskauer reaction, positive.

TABLE 1.—*Results of Fermentation-Sugar Tests*

	24 Hours	48 Hours	72 Hours
Glucose	Acid and gas	Acid and gas	Acid and gas
Maltose	Acid and gas	Acid and gas	Acid and gas
Lactose	Acid and gas	Acid and gas	Acid and gas
Mannite	Acid and gas	Acid and gas	Acid and gas
Saccharose	Acid and gas	Acid and gas	Acid and gas

ANIMAL INOCULATION

Oct. 3, 1923, Guinea-Pig 1 was given a 1 c.c. intraperitoneal injection of an emulsion of the biopsy section of the skin from the face of Miss K. Guinea-Pig 2 was given a 2 c.c. injection.

Guinea-Pig 1 remained apparently normal for two months. Guinea-Pig 2 remained apparently normal for twenty-two days, when there appeared over the back and parasternum, abundant small, elevated, crusted lesions, the crusts being dark red from dried blood. Owing to the hairy covering of the skin, the probabilities are that the lesions were not discovered in their early incipiency. Removal of the crusts disclosed a deep ulcerating surface. The

Fig. 4.—Eruption in guinea-pig produced by intraperitoneal inoculation of an emulsion of an acnitis nodule.

lesions appeared to increase in number and size until Nov. 1, 1923, when the animal died. Examination of the skin for parasites and fungi was negative.

At the necropsy of Guinea-Pig 2, the lesions on the skin were irregular reddish brown to blackish crusts, sometimes in linear form. These appeared to represent desiccated pustules. Irregular ulcerations with sharp edges were present. The entire back was almost completely denuded. Where each lesion appeared in the skin, the subcutaneous tissue had slight hemorrhage, and ulcerations extended through the skin, reaching the subcutaneous tissues.

The inguinal lymph glands were slightly enlarged; there was no hemorrhagic edema. The lung, liver, spleen and other organs appeared apparently normal. A section of the skin of the guinea-pig was removed and fixed in 10 per cent. formaldehyd for pathologic study. Another section was emulsified and used for culture tests and guinea-pig inoculation.

Histopathologic Examination of Guinea-Pigs.—As nothing but dried crusts and ulcerations were present at necropsy, the histologic study of the skin was rather unsatisfactory. There was a marked cellular infiltration following the blood vessels and around the hair follicles. The blood vessels and lymph paths were dilated. No giant cells were seen.

Guinea-Pig Inoculation of Emulsion of the Skin of Guinea-Pig 2.—Nov. 1, 1923, Guinea-Pig 3 received an intraperitoneal injection of 1 c.c. of an emulsion of a specimen removed from Guinea-Pig 2 at necropsy. Guinea-Pig 4 received 2 c.c. Both guinea-pigs remained apparently normal for three months.

Bacteriologic Examination of the Heart Blood and Skin of Guinea-Pig 2.—Anaerobic cultures of the heart blood were made in hormone brain broth, containing 0.1 per cent. glucose. They were incubated for forty-eight hours at 37.5 C. During the first twenty-four hours, a marked even turbidity of the medium, with no surface growth, was observed; later, a growth was precipitated as a flocculent sediment of considerable amount. Microscopic examination revealed a small coccus, single and in twos and threes, which was gram-positive.

Cultures on hormone blood agar revealed a scanty growth, filiform, iridescent, raised, with a tendency to form minute, round convex colonies; there was no hemolysis, but the blood agar surrounding the colony and the edge of the growth became somewhat dark green.

Microscopic examination of these cultures revealed a small coccus, mostly single, and gram-positive. It was identified as the *Streptococcus viridans.*

For anaerobic culture of the skin lesions of Guinea-Pig 2, an area of the affected skin approximately one-half inch square was emulsified in hormone broth and a culture was made in hormone brain broth containing 0.1 per cent. glucose. It was incubated at 37.5 C. for five days. The microscopic examination of this broth emulsion, stained with methylene blue and Gram stain, revealed a short gram-negative rod, gram-positive cocci and a large gram-positive rod. Staining by the acid-fast method did not reveal any organisms retaining the fuchsin stain. The anaerobic hormone brain broth cultures were turbid, showed ring formation and a heavy flocculent sediment.

On microscopic examination, the growth stained with Gram stain revealed: (*a*) a small gram-positive coccus in short chains; (*b*) *a short gram-negative rod*, mostly single but also in pairs end to end; (*c*) a medium sized coccus, single and in bunches which was gram-positive; (*d*) a large rod which was gram-positive, with rounded ends and spore formation.

Hormone blood agar plates of a skin culture from Guinea-Pig 2, revealed the following colonies:

Colony 1: This was minute, round, with a smooth surface, umbonate (having a button-like raised center), edge entire and iridescent; there was a slight greening of medium surrounding the colony. Microscopic examination revealed a small coccus, single and in short chains of three and four, which was gram-positive.

Culture of Colony 1: There was a scanty growth, filiform, iridescent, raised, glistening, with individual colonies coalesced, there was no odor, and the medium appeared somewhat green. Microscopic examination showed a small coccus, single and in short chains of three and four, which was gram-positive and was identified as *Streptococcus viridans.*

Colony 2: This was moderate sized, round, with a smooth surface, convex, edge entire, yellowish-gray to translucent and somewhat moist; there was no hemolysis or change in blood agar medium. Microscopic examination showed a small rod, with a length of from 2.5 to 4 microns, and a width of from

0.5 to 0.8 microns, more or less uniform in size, single but often in pairs end to end, rounded ends, evenly stained, no spores, no capsules, which was gram-negative.

Culture of Colony 2: This was a moderate growth, filiform, raised, glistening, smooth, translucent, no pigment, slight musty odor, of viscid consistency; the medium was not changed and there was no hemolysis. Microscopic examination revealed *a small rod*, with a length of from 2.5 to 4 microns, and a width of from 0.5 to 0.8 microns, some forms appeared larger, mostly single, rounded ends, evenly stained and gram-negative.

Grown in hormone bouillon this organism also manifested the same properties as Culture 3, isolated from the emulsion of the lesion of Miss K., in that it appeared larger and had a greater tendency to form short chains and also showed bipolar staining. It also conformed to the other biologic characteristics of that organism, such as being motile, not liquefying gelatin, fermenting glucose, lactose, saccharose, maltose and mannite.

Colony 3: This colony was moderate sized, round, smooth, convex, edge entire, white, opaque; there was no change in the medium and no hemolysis. Microscopic examination revealed a coccus, which was medium sized, single and in bunches, and gram-positive.

Cultures of Colony 3: This was a moderate growth, filiform, raised, white, opaque, somewhat shiny, the medium was not changed and there was no hemolysis. Microscopic examination revealed a medium sized coccus, single and in bunches, which was gram-positive. It was identified as *Staphylococcus albus*.

Colony 4: There was a rapid filamentous growth on the surface of the plate; it was flat and somewhat dry on the surface. Microscopic examination revealed a large rod, the length of which was approximately two and one-half times the breadth, with rounded ends, single and in twos and threes end to end, rounded ends, spore formation; it was gram-positive.

Culture of Colony 4: This was a moderate, spreading growth, covering the whole surface of the blood agar slant, flat, somewhat dull, easily removed from the medium; the medium was not changed. Microscopic examination revealed a large rod, the length of which was approximately two and one-half times its breadth, with rounded ends, single and in chains of two and three, rounded ends, spore formation; gram-positive. It was identified as *Bacillus subtilis*.

IMMUNOLOGIC STUDIES TO DETERMINE WHETHER ANTIBODIES FOR ORGANISMS ISOLATED FROM SKIN LESIONS OF PATIENT WERE CONTAINED IN PATIENT'S SERUM

TABLE 2.—*Agglutination Test*

Antigen	1:5	1:10	1:20	1:40	1:80	1:160	Antigen Control
Colony 1	—	—	—	—	—	—	Normal serum
Colony 2	—	—	—	—	—	—	
Colony 3	—	—	—	—	—	—	
Colony 1	—	—	—	—	—	—	Patient's serum
Colony 2	—	—	—	—	—	—	
Colony 3	—	—	—	—	—	—	

TABLE 3.—*Complement-Fixation Test*

	Dose						Serum		
	0.1	0.05	0.025	0.012	0.006	0.003	S. C. 0.1	A. C.	C. C.
Patient's serum	+3	+1	—	—	—	—	—	O.K.	O.K.
Normal control serum	—	—	—	—	—	—	—	..	..

The antigen used in the complement-fixation test consisted of a heavy suspension of Colony 3 (*gram-negative rod*) in 0.85 per cent. of salt solution, killed by heat.

EFFORTS TO PRODUCE SKIN LESIONS IN GUINEA-PIG BY INJECTIONS OF A SUSPENSION OF THE ORGANISMS ISOLATED FROM SKIN LESIONS OF PATIENT

On Nov. 1, 1923, a suspension of twenty-four hour cultures of Colonies 1, 2 and 3 was prepared by removing the growth from blood agar slants and suspending it in 0.85 per cent. sodium chlorid solution, mixed in equal proportions. Guinea-Pigs 5 and 6 were inoculated intraperitoneally with 1 c.c. of this suspension.

Guinea-Pig 6 died in twenty-two hours, and necropsy revealed a marked injection of all of the subcutaneous blood vessels. The lungs were mottled red, and edematous; the peritoneum was thickened, rough and exhibited many small petechiae; the liver was dark brown, with edges rounded; the spleen was considerably enlarged with several dark red, elevated areas on the surface. The omentum had a mottled, red appearance with multiple petechiae; in the intestines, there was marked injection of all capillaries, and they were greatly distended with gas. Abdominal lymph glands were mottled, dark red and enlarged. The peritoneal cavity contained approximately 5 c.c. of a yellowish-red, viscid fluid.

Microscopic examination of the heart blood revealed many *small rods* in clumps, which were gram-negative. Microscopic examination of the peritoneal fluid revealed apparently only one type of organism that was a short rod, the length of which was approximately twice the breadth; the organisms were single and in pairs; some appeared to be stained bipolar. They were gram-negative.

Cultures of the heart blood of Guinea-Pig 6 on hormone blood agar plates revealed many moderate sized colonies, round, smooth, entire, convex, and yellow-white to translucent; there was no hemolysis or coloring of the medium. Microscopic examination revealed a *short rod,* with a length of from 2.5 to 4 microns, and a width of from 0.5 to 0.8 microns, with rounded ends, single and in pairs, some in chains of three and four, motile, no spores, evenly stained.

Cultures on hormone blood agar slants gave a moderate filiform growth, raised, glistening, smooth, translucent, somewhat viscid. Microscopic examination was the same as that of the colony. The cultures of the peritoneal fluid revealed an organism with characteristics similar to that of the organism isolated from the heart blood. These two organisms gave biologic reactions identical with those shown by Colony 3 (*Bacillus x*) isolated from the skin lesion of the patient, which was injected into this guinea-pig in combination with the other two organisms. Guinea-pig 5 survived for three months, presenting no symptoms beyond a slight dulness for twenty-four hours after injection.

INOCULATION OF SEPARATE ORGANISMS ISOLATED FROM SKIN LESIONS OF PATIENT INTO GUINEA-PIGS IN AN EFFORT TO PRODUCE ACNITIS-LIKE LESIONS

On Nov. 31, 1924, Guinea-Pig 7 was given 2 c.c. of a suspension of Colony 1 (*Staphylococcus albus*), intraperitoneally. Guinea-Pig 8 received 1 c.c. of a suspension of Colony 1 (*Staphylococcus albus*), intraperitoneally. Guinea-Pig 9 received 2 c.c. of a suspension of Colony 2 (*Micrococcus tetragenous*), intraperitoneally. Guinea-Pig 10 received 1 c.c. of the same suspension. Guinea-Pig 11 received 2 c.c. of a suspension of Colony 3 (*Bacillus x*), intraperitoneally. Guinea-Pig 12 received 1 c.c. of the latter suspension.

The hair over the back of the guinea-pigs was removed at intervals with barium sulphid, so that if any lesions appeared they could be readily recognized.

Guinea-Pigs 7, 8, 9 and 10 remained apparently normal and manifested no symptoms or lesions for a period of three months.

Guinea-Pigs 11 and 12, injected with the gram-negative rod, died in forty-eight hours. Necropsy of both guinea-pigs presented a typical picture of septicemia, a purulent peritonitis being the outstanding lesion produced. This necropsy was identical with that of Guinea-Pig 6, which received injections of a mixture of the organisms mentioned above.

Heart blood cultures and peritoneal fluid cultures revealed an organism in pure culture having the same biologic characteristics as that injected, i. e., the same as the gram-negative rod (*Bacillus x*).

VIRULENCE DETERMINATION OF COLONY 3 (GRAM-NEGATIVE ROD) (BACILLUS X) AND AT THE SAME TIME DETERMINATION WHETHER SUBLETHAL DOSES WOULD PRODUCE SKIN LESIONS

The following guinea-pigs, and rabbits received injections of twenty-four hour bouillon cultures of Colony 3 by the methods indicated: Guinea-Pig 13 received 0.1 c.c. and four days later 0.3 c.c. intraperitoneally. Guinea-Pig 14 received 0.1 c.c. and four days later 0.5 c.c. intraperitoneally. Guinea-Pig 15 received 0.5 c.c. intraperitoneally. The same amount was injected four days later. Guinea-Pig 16 received 0.1 c.c. subcutaneously and four days later 0.5 c.c. subcutaneously. Guinea-Pig 17 received 0.1 c.c. subcutaneously and four days later 0.3 c.c. subcutaneously. Rabbit A was given 0.3 c.c. intratesticularly. Rabbit B (white) was given 0.5 c.c. intravenously and 0.05 c.c. in the right ear intracutaneously.

RESULTS OF ANIMAL INOCULATION FOR VIRULENCE

Guinea-Pig 13 remained apparently normal for three months. Guinea-Pig 14 died in six days, from purulent peritonitis and septicemia. Guinea-Pig 15 died in three days from purulent peritonitis and septicemia. Guinea-Pig 16 died in twelve days from lesions indicative of septicemia. Guinea-Pig 17 remained apparently normal for three months. Rabbit A remained apparently normal for three months. There was mild orchitis for forty-eight hours, which gradually disappeared. Rabbit B died in twelve days from general septicemia.

Necropsy of all the guinea-pigs that died — Nos. 14, 15 and 16 — was identical with the necropsies of the guinea-pigs previously receiving injections with this organism, and described. In every instance, the heart blood cultures revealed in pure culture the organism injected. Guinea-Pig 17, receiving subcutaneous

injections, did not show a purulent peritonitis like the guinea-pigs receiving intraperitoneal injections, but the lesions of the internal organs were similar. Little tissue change besides a slight thickening of the subcutis was noted at the site of the injection of Guinea-Pig 17.

The guinea-pigs remaining normal, Nos. 13 and 17, presented no skin lesions and apparently were not inconvenienced by the injection. Neither was Rabbit A, into the testis of which injections of 0.3 c.c. of bouillon culture were made.

Rabbit B which received 0.5 c.c. injections of bouillon culture died in twelve days. This rabbit was extremely sick during this whole period. Six days after injection, it became paralyzed in the hind legs. It had no control over urination and defecation. There was a purulent discharge from the eyes and nose, yet the appetite remained fairly good. On the eighth day, it became semicomatose and gradually passed into a coma, and died on the twelfth day.

At necropsy no lesions were observed on the skin, but when the skin was removed, two areas of subcutaneous hemorrhage—approximately 5 by 1 cm. and 1 cm. square were observed over the abdomen. This hemorrhage did not penetrate into the skin. The lymph glands were considerably enlarged; the lungs presented large areas of consolidation. The liver was dark brown and swollen; the spleen was considerably enlarged and dark red. The peritoneum was rough, moist and markedly injected. The abdominal cavity contained little fluid; the intestines showed catarrhal enteritis.

Cultures of heart blood, lungs, liver, spleen and peritoneum of Rabbit B revealed a pure culture of the organism injected, conforming in its biologic characteristics with Colony 3 of the cultures of the skin of the patient.

The two hemorrhagic areas in the abdominal subcutis did not reveal the organism on culture. These hemorrhagic areas were possibly traumatic and due to the handling of the animal or the position in which the animal lay while in coma.

The intracutaneous injection of 0.05 c.c. revealed a small, elevated, red area during the first forty-eight hours, approximately 1 cm. in diameter, later decreasing in size and developing a hard, somewhat yellow center.

Second Biopsy of Skin Lesion of Patient.—On November 11, the patient returned for a second resection of a skin lesion. A small lesion was removed from the left cheek and emulsified in hormone broth. Anaerobic and aerobic cultures were made in hormone broth brain medium, and guinea-pigs were also given injections, the hair being removed at intervals to observe any development of skin lesions.

Guinea-Pig 18 was given 1 c.c. intraperitoneally and died in eleven days. There were no skin lesions. Guinea-Pig 19 was given 1 c.c. intraperitoneally, and remained apparently normal for three months. Guinea-Pig 20 was given 1 c.c. intraperitoneally, and remained apparently normal for three months. Guinea-Pig 21 was given 1 c.c. intraperitoneally, and remained apparently normal for three months.

At necropsy, Guinea-Pig 18, which had appeared in good health up to the day of death, was found not to be emaciated, and had a fair amount of subcutaneous fat. The lungs, liver and spleen appeared apparently normal. The intestines contained considerable gas, and the capillaries were considerably injected. The intestinal mucosa was swollen and rough and covered with a light layer of mucous material.

Cultures of the heart blood in hormone brain broth were sterile. Death in this guinea-pig was apparently due to some intestinal disturbance rather than to the material injected.

Cultures of Broth Emulsion of Skin Removed from the Patient.—Cultures of the emulsion of a skin lesion of the patient were made in hormone brain broth, containing 0.1 per cent. glucose and incubated anaerobically and aerobically at 37.5 C. for seventy-two hours.

Anaerobic Cultures: Microscopic examination stained by the Gram method revealed the following organisms: (*a*) moderate sized cocci, single and in small bunches, gram-positive; (*b*) moderate sized cocci but smaller than the foregoing, appearing in chains of six and eight, gram-positive.

Hormone blood agar plates of the anaerobic cultures grew the following colonies:

Colony 1: This was of moderate size, round, convex, smooth, edge entire, white, opaque; there was no change of mediums nor hemolysis. Microscopic examination revealed a moderate sized coccus, bunched and gram-positive.

Culture of Colony 1: There was a moderate growth in twenty-four hours, filiform, raised, glistening, smooth, white, opaque, somewhat raised, and the medium was not changed. Microscopic examination revealed a moderate sized coccus, in bunches, gram-positive, which was identified as *Staphylococcus albus.*

Colony 2: This was a minute colony, round, convex, edge entire, iridescent. A small, somewhat green area was seen around the colony. Microscopic examination revealed a small coccus, in short chains of three to six, also bunched, which was gram-positive.

Cultures of Colony 2: There was a scanty growth in twenty-four hours, filiform, raised, with a tendency to colony formation, glistening, iridescent. The medium surrounding the growth was of greenish appearance. Microscopic examination showed a small coccus, in chains of three to six, a few longer, which was gram-positive. It was identified as *Streptococcus viridans.* In hormone bouillon, Colony 2 gave long chains of fifteen to twenty-five.

Comment.—It is to be noted that the second examination of the skin lesion of the patient did not reveal the small gram-negative rod isolated in the first examination.

DISCUSSION

Let us briefly recapitulate the findings.

Smears from an open lesion of acnitis examined in two laboratories at different times were independently reported to reveal the presence of staphylococci and a gram-negative, rod-shaped organism, which for convenience and brevity we shall call *Bacillus x.*

A fragment of a nonulcerated nodule grown in a special anaerobic medium yielded three organisms, one of which was *Bacillus x.* This bacterium did not primarily grow in aerobic cultures. An emulsion of the excised nodule injected into the peritoneal cavity of two guinea-pigs produced in the animal receiving the larger dose a generalized pustulocrustaceous eruption followed by ulceration, appearing on the twenty-second day. *Bacillus x* was recovered in culture from the cutaneous lesions and from the peritoneum and heart blood. The emulsion of the skin of this guinea-pig failed to produce a similar condition in further inoculations. Efforts to produce an eruption in guinea-pigs by the intraperitoneal and intravenous injection of a culture of *Bacillus x* failed,

although the organism was virulent and caused death in both guinea-pigs and rabbits. Agglutination tests carried out with *Bacillus x* and the patient's blood serum were negative. The complement-fixation test, however, made with the patient's serum and an antigen consisting of a heavy suspension of *Bacillus x* in salt solution gave a distinctly positive reaction— + 3, + 1. With a normal control serum, the test was negative.

It should be added that the inoculation of a second nodule removed failed to produce an eruption and failed to yield *Bacillus x*, but the eruption was at this time on the decline.

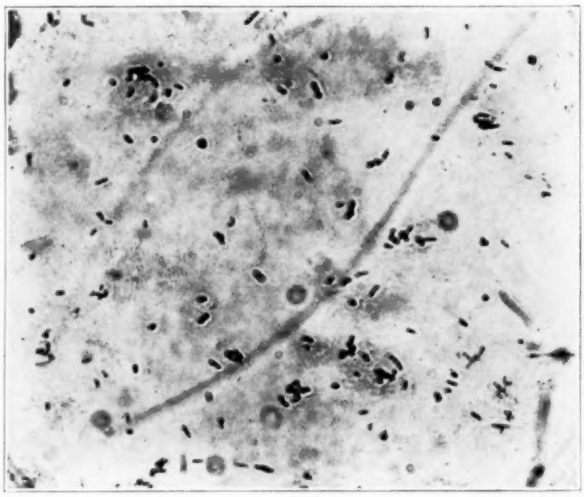

Fig. 5.—*Bacillus x* isolated from case of acnitis; magnification, × 950.

Bacillus x obviously belongs to the colon group, but it differs from the ordinary colon bacillus in its virulence for animals and in certain cultural and biologic characteristics. *It is significant to note that none of the inoculated animals showed any evidence of tuberculosis.*

From all that we know of acnitis, it is an acute and probably a self limited disease coming on with suddenness and characterized by repeated eruptive crops. In some cases, a general disturbance with fever marks the onset. That it is an infectious granuloma, there can be little doubt.

We are desirous that any one who encounters a case of acnitis should repeat the experimental work here detailed to determine whether the results corroborate our findings. The least complicated and most important examination would be the culture in Rosenow's anaerobic brain medium.

TABLE 4.—*Characteristics of Bacillus x Isolated from Acnitis Case Compared with B. coli-communior and B. coli-communis*

	Bacillus x	B. coli-communior*	B. coli-communis*
Morphology	Gram-negative rod	Gram-negative rod	Gram-negative rod
Motility	Motile	Motile	Motile
Gelatin	Not liquefied	Not liquefied	Not liquefied
Litmus milk:			
1 day	Acid	Acid	Acid
2 days	Acid	Acid	Acid
3 days	Acid No coagulation	Acid Coagulation	Acid Coagulatoin
Sugar fermentation:			
Glucose	Acid and gas	Acid and gas	Acid and gas
Lactose	Acid and gas	Acid and gas	Acid and gas
Maltose	Acid and gas	Acid and gas	Acid and gas
Saccharose	Acid and gas	Acid and gas	No acid or gas
Mannite	Acid and gas	Acid and gas	Acid and gas
Dulcite	Acid and gas	Acid and gas	Acid and gas
Russell's double sugar	Butt: Acid-gas Slant: Acid	Butt: Acid-gas Slant: Acid	Butt: Acid-gas Slant: Acid
Indol	Not produced	Produced	Produced
Nitrate reduction	Reduced to nitrites	Reduced to nitrites	Reduced to nitrites
Voges-Proskauer reaction	Positive	Negative	Negative
Methyl red	Positive	Positive	Positive
Neutral red	Reduced	Reduced	Reduced

* From current textbooks on bacteriology.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: This paper is very suggestive, especially when we consider it with Dr. Guy's paper of last year in connection with the finding of other than tuberculous germs in the cases of papulonecrotic tuberculid. The most interesting thing to my mind is that the picture microscopically so closely resembles tuberculosis, and yet we can be safe in assuming that the tubercle bacillus has nothing to do with it. I think it is worthy of note that many conditions that closely resemble tuberculosis have no relation to the tubercle bacillus. Foreign bodies are likely to produce a tuberculous-like structure. We have a case that was thought to be a true tuberculosis, so strikingly similar was it to that condition that many pathologists passed it as such, but it turned out to be a foreign body irritation from cactus spines in a patient who was sent to southern California for treatment for pulmonary tuberculosis.

DR. FREDERICK D. WEIDMAN, Philadelphia: Dr. Max Strumia conducted some experiments in regard to etiology on two cases of acne varioliformis at the University of Pennsylvania, in which he has fulfilled all of Koch's postulates. In both of these, in addition to the staphylococcus he has isolated a streptococcus, and the latter he has run through the usual fermentation reactions and identified as the streptococcus of Rosenbach. He has produced acne varioliformis lesions in guinea-pigs, both by intradermal injections into the skin and also by rubbing into the skin, producing lesions which were ecthymatiform in all those cases in which he introduced the staphylococcus and streptococcus together. This symbiosis seemed to be necessary for the production of deep ecthymatiform lesions. He thinks that in order to produce these characteristic lesions surrounded by the proper zone of edema there must be two factors present, one of which should be necrosis-producing, and another, which perhaps furnishes some pabulum for the essential agent producing the disease. To test this out, he took croton oil (and turpentine) and

injected it with the staphylococci into guinea-pigs and induced lesions that were approximately of the same type as those seen in human acne varioliformis.

He has also reproduced the lesion on the patient himself with stock cultures of mixed streptococcus and staphylococcus.

I believe that in these diseases acne varioliformis, acnitis and papulonecrotic tuberculid—we do not have to do with any one type of organism; and, on the other hand, we know that many different organisms may produce the same type of lesion; for example, the ordinary furuncle can be excited by different organisms, so that we can never say that this or that organism always produces a certain kind of lesion. These may well be clinical entities, but they are not necessarily pathologic entities. We cannot say that some certain organisms must cause acnitis and others acne varioliformis, etc. In the case of Dr. Schamberg's presentation, very likely this *Bacillus x* is one of several that can produce acnitis.

In connection with the foreign body tubercle formation, I can vouch that those who do much histologic work frequently encounter cases in which the lesions of tuberculosis are simulated by foreign body reaction, and there may be great difficulty in making the differentiation. We have been doing some experimental cholesterol work, and the morphology of tuberculosis may be imitated closely in many lesions. Highman pointed out long ago the limitations of histology in dermatoses. The histology seldom reveals the cause.

The final criterion as to whether we have experimentally reproduced acne varioliformis or acnitis is to reproduce the distribution of the disease; but in the animal, as Dr. Schamberg said, we cannot expect to do this, and it is unpractical and inadvisable to attempt to do this in the human subject. We encounter severe and unfortunate limitations here. But after all is said and done, I still feel certain that various organisms may produce this disease; and we must not become obsessed with the idea that simply because an organism has produced a certain lesion, it is the one which must produce it in all cases.

Dr. Jay Frank Schamberg, Philadelphia: I agree with the tenor of the discussion of Dr. Wile and of Dr. Weidman. We did not, of course, pretend to draw the conclusion that this organism was the cause of the acnitis in the case we described, but there were certain suggestive features, one of which I will emphasize. The lesions in the guinea-pig did not result from cutaneous inoculation of an emulsion of the excised lesion, but from intraperitoneal injection. If it produced the eruption in the skin, it must have had an affinity for the skin; a septic and fatal infection was produced. When one rubs or injects various organisms into the skin, there may be dermatitis or other cutaneous manifestations induced which may not be specific.

We present our findings for what they are worth with the hope that others may either confirm or deny them.

THE CULTURAL REQUIREMENTS OF THE ACNE BACILLUS

WITH SPECIAL REFERENCE TO THE HYDROGEN-ION CONCENTRATION OF THE MEDIUMS MOST SUITABLE FOR ITS GROWTH, WITH A NOTE ON AN UNIDENTIFIED BACILLUS OCCASIONALLY ASSOCIATED WITH IT *

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The acne bacillus is a gram-positive, diphtheroid organism found in comedones, in the contents of acne lesions and in seborrheic filaments. In 1893, the bacillus was first noticed by Unna [1] in smears from comedones, but he did not cultivate it. In the following year, Hodara,[2] working in Unna's laboratory, succeeded in obtaining slight growth of the organism on agar plates, but was unable to transfer it. In 1897, Sabouraud [3] isolated it on a special acid glycerin agar by planting the central portion of seborrheic filaments on the surface of slants. Contamination with staphylococci always occurred, but these organisms were disposed of by allowing the cultures to stand several weeks or by heating them for ten hours at 65 C. In 1899, Gilchrist [4] obtained the organism, often in pure culture, directly from acne nodules by planting the gelatinous contents on an acid glycerin agar. He demonstrated that the blood of patients with severe acne agglutinated the acne bacillus, and that the organism was pathogenic for animals. All these investigators used aerobic methods of cultivation.

Hallé and Civatte,[5] in 1897, were apparently the first to succeed in isolating and growing the acne bacillus by anaerobic methods. They used dextrose agar in deep shake tubes for obtaining pure cultures, and

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1. Unna: The Histopathology of the Diseases of the Skin, 1896.
2. Hodara: Monatschr. f. prakt. Dermat. **18**:573, 1894.
3. Sabouraud: Les maladies séborrhéiques, Paris, 1902.
4. Gilchrist: Johns Hopkins Hosp. Rep. **9**:409, 1900; J. Cutan. Dis. **21**:107, 1903.
5. Hallé and Civatte: Ann. de dermat et syph. **8**:185, 1907.

subcultures were made on Sabouraud's glycerin agar or on dextrose agar. They were unable to obtain any growth by aerobic methods of cultivation.

In 1902, 1904 and 1908 Engman [6] succeeded in growing the organism aerobically. He found a nutrient agar, neutral or slightly acid in reaction to be the best medium. Fleming,[7] in 1909, using aerobic methods, cultivated the bacillus on acid or on acid glycerin agar. Better growth, however, was obtained by the addition of 0.1 per cent. oleic acid to the glycerin agar. In the same year, Hartwell and Streter [8] were able to grow the bacillus anaerobically on all the common laboratory mediums and aerobically on acid agar.

Südmersen and Thompson,[9] in 1910, found that the best medium for growing the organism was acid blood agar or serum agar. Growth was first obtained under anaerobic conditions, but after several transfers it grew equally well under aerobic conditions. In the same year, Molesworth [10] employed 2 per cent. dextrose agar in deep shake tubes for isolating the bacillus, and the same medium in slants for subcultivating it. He used anaerobic methods, and concluded that this was the essential factor in successful cultivation, and that no special mediums were necessary. Lovejoy and Hastings,[11] in 1911, found that the organism grew well either on plain or on 2 per cent. glucose agar.

Other investigators, however, have been unable to obtain any growth of the acne bacillus, and Gilchrist, since the publication of his work, has obtained mediums from the laboratory, supposed to have been prepared in the same manner as that previously used by him, but on which the organism would not grow. Engman also states that he has repeatedly been unable to obtain growth on batches of mediums made up in the same manner as others on which the organism would grow luxuriantly.

It would appear, from the foregoing investigations, that for its best growth the acne bacillus must require mediums differing in certain respects from the standard laboratory varieties. Although some of the investigators say nothing concerning the reaction of the medium which they have employed, in the majority of cases, it has been acid. Südmersen and Thompson have attempted to establish the acidity of the mediums which are best suited to the growth of the organism. This they state

6. Engman: Interstate M. J. **17**:943, 1910.
7. Fleming: Lancet **1**:1035, 1909.
8. Hartwell and Streter: Boston M. & S. J. **161**:882, 1909.
9. Südmersen and Thompson: J. Path. & Bacteriol. **14**:224, 1910.
10. Molesworth: Brit. M. J. **1**:1927, 1910.
11. Lovejoy and Hastings: J. Cutan. Dis. **29**:80, 1911.

to be + 40[12] to phenolphthalein. Molesworth, however, was unable to obtain a solid agar which had been acidified to this degree.

It was with the desire of helping to standardize a medium, with special reference to its hydrogen-ion concentration, on which the acne bacillus could be uniformly isolated and cultivated, as well as studying some of its cultural characteristics both aerobically and anaerobically that our investigations were undertaken.

METHODS OF OBTAINING CULTURES

Technic and Mediums.—Our first attempts to grow the organism were made by planting seborrheic filaments from the nose on 2 per cent. glycerin agar slants[13] and incubating aerobically. The nose was washed with alcohol, and the filaments expressed with the finger tips. These were then removed with a straight platinum needle and planted on the surface of the agar slants, the needle being pushed down into the medium so as partially to bury the filament. Various lots of mediums were used varying in p_H from 5 to 8. Growth was frequently obtained but usually on the medium with a p_H somewhere between 6 and 7. We then tried 1 per cent. dextrose agar and 2 per cent. glycerin agar, to which 0.1 per cent. oleic acid had been added, as recommended by Fleming.[14] The results were practically identical with those obtained with the 2 per cent. glycerin. After roughly determining that a p_H of 6.4 or 6.6 was near the correct acidity for the mediums, we tried transplanting loopfuls of pus or the granular contents of acne papules or nodules in the same manner as had been used with the seborrheic filaments. Positive cultures were frequently obtained.

Anaerobic methods were next investigated. The same mediums and methods of inoculation were used as in the aerobic cultivation of the organism. The tubes were rendered anaerobic by the pyrogallic-acid-sodium hydrate method, as recommended by Wright. Positive cultures were much more frequently obtained and growth was more luxuriant than when aerobic methods were used.

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12. We believe that this must have been a misprint, and that + 4.0 is more likely to be what the authors meant.

13. We used the stock laboratory supply of meat infusion agar prepared in the standard way. (Hiss, Zinsser and Russell: Textbook of Bacteriology, New York, 1923). It usually had an initial p_H value of from 7 to 7.8. It was readjusted with sterile precautions to the desired acidity with hydrochloric acid, although in a few instances we used acetic acid, citric acid and in one case butyric acid. In growing the bacillus, no apparent advantage was obtained by substituting the three latter acids for hydrochloric acid. Sterile glycerin or sugar solution when required was added to the agar before adjusting the p_H. The medium was not resterilized.

14. Hereafter this medium is referred to as Fleming's medium.

We were next successful in isolating the organism from deep 1 per cent. dextrose agar shake tubes. The same meat infusion agar was employed as for slants, or the agar concentration was reduced to 1 per cent. The tubes were seeded at from 45 to 50 C. in successive dilution with emulsions of seborrheic filaments or material from acne lesions.

Results and Character of Growth.—When cultivating the bacillus on slanted solid mediums, contamination with staphylococci was frequent, although we often obtained apparently pure growths. The staphylococci appear after twenty-four hours, forming a thin whitish mantle around the transplanted material. After five or ten days, the acne bacillus, if it grows, makes its appearance as a beadlike or oval, heaped-up projection from the edge or beneath the inoculum, pushing itself up through the mantle of staphylococci, if these are present. The color is at first whitish or dark gray, later assuming, in the majority of instances, a brownish tint.

If anaerobic methods are used, evidence of staphylococcic contamination is much less frequently present, although it may occasionally become evident when aerobic transplants are made. The colonies of bacilli appear sooner with this method, and the growth is much more luxuriant, often developing from two or three points in the transplant. Positive results are much more frequently obtained; at one time we secured fifteen cultures from sixteen seborrheic filaments, and pigmentation is much more intense than in aerobic cultivation. The color varies from a dark gray through different shades of pink to a deep red.

Pure cultures may be obtained by allowing the tubes to stand at room temperature for five or six weeks, as recommended by Sabouraud, since during this time the staphylococci will die, or the organisms may be separated in shake tubes. If 1 per cent. dextrose or 2 per cent. glycerin deep agar shake tubes are used to isolate the bacillus, staphylococci, if present, appear much sooner than the colonies of the acne bacillus. After one or two weeks, however, the colonies of the two organisms are easily distinguished. (The growth and appearance of the acne bacillus in deep shake tubes will be more fully described in the discussion of cultural characteristics.)

DETERMINATION OF THE HYDROGEN-ION CONCENTRATION OF MEDIUMS MOST SUITABLE FOR THE GROWTH OF ACNE BACILLUS

After our first experience in isolating the acne bacillus on mediums of different p_H concentrations, and after we had isolated a sufficient number of strains, the following experiment was carried out in order more definitely to establish the p_H of the mediums required for the maximal growth.

Series of deep shake tubes of 1 per cent. dextrose infusion agar were prepared with the following p_H: 5.4, 5.8, 6.2, 6.6, 7, 7.4, 7.8. Three tubes of each p_H were inoculated in successive dilutions with strains A, E, G, M, N, P and Y. A series was also inoculated with an emulsion from seborrheic filaments.

The seeding was very heavy in the first dilutions. After forty-eight hours' incubation, a cloudiness of the first tubes of all the strains was

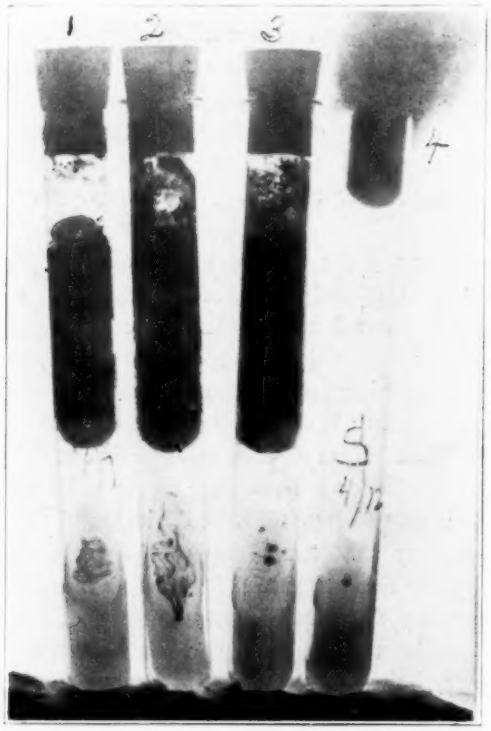

Fig. 1.—Tubes 1, 2 and 3 are anaerobic cultures of the acne bacillus. Tube 4 is an aerobic culture. In Tube 3, conditions have not been favorable for development of the organism, and growth has taken place only at certain points.

present in the hydrogen-ion concentrations of 6.2, 6.6 and 7. The 5.4 and the 7.8 p_H series showed no evidence of growth in any of the tubes. Strains P, Y, E, M and N showed growth in the first tubes of p_H 5.8, and E and M showed a slight cloudiness of the medium in the 7.4 p_H. No growth was evident in the second and third dilutions except with strains P and Y, each of which showed a narrow band of colonies from 1 to 2 cm. below the surface of agar in the p_H 6.2, 6.6 and 7.

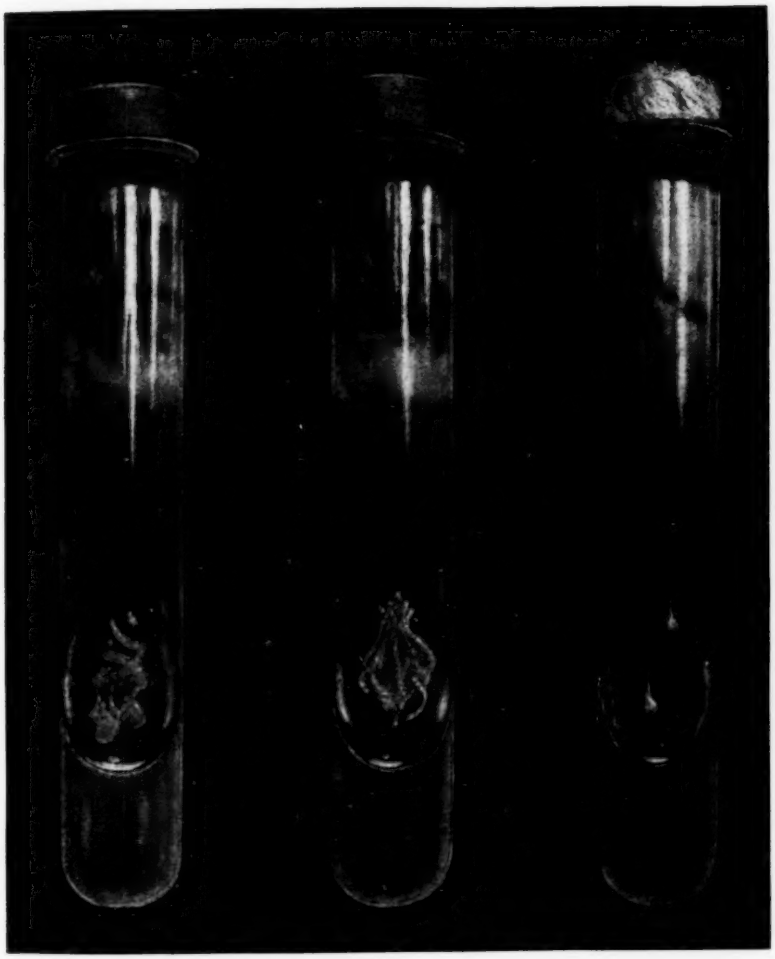

Fig. 2.—Cultures of the acne bacillus on 1 per cent. dextrose agar, p_H 6.6, showing character of growth and pigment formation. The tube on the right is an aerobic culture, the other two anaerobic cultures.

After four days' incubation, growth became well marked in the second and third dilutions of all the strains in the p_H from 6.2 to 7, inclusive, with some of the strains showing development in the 5.8.

After ten days, there was some extension of the range of growth toward the acid and also toward the alkaline side. In general, however, the growth was better at p_H 6.2 and 6.6, with a slight falling off at 7 and 5.8.

The series inoculated with the emulsion of seborrheic filaments corresponded in general with the foregoing. All of the tubes were watched for several weeks, during which there was no apparent growth in the p_H 7.8 tubes, but some of the p_H 7.4 and 5.4 tubes showed growth in the first dilutions.

On slant agar, however, with a p_H of 7.8, we obtained some growth from all of our ten strains anaerobically. It was thin and poorly nourished, however, and did not show the characteristic heaping up and pigment formation. Aerobically, only four of the strains showed any apparent increase in the size of the transplant.

CULTURAL CHARACTERISTICS

Source of Strains.—Ten strains were used for subcultural study. The p_H of the mediums on which the strains were isolated varied from 6.2 to 6.8, unless otherwise stated.

Strain A: This was obtained aerobically on 2 per cent. glycerin agar from a seborrheic filament from a patient who had never had acne.

Strain E: This was obtained anaerobically from the same patient and on the same mediums as Strain A.

Strain G: This was obtained anaerobically on 1 per cent. dextrose agar from a pustule on the chin of a patient with acne rosacea.

Strain K: This was obtained anaerobically on 2 per cent. glycerin agar from a nodule on the back of a patient with extensive acne.

Strain M: This was obtained aerobically on 2 per cent. glycerin agar from a small acne papule on the chin of a patient with mild acne.

Strain N: This was obtained aerobically on Fleming's medium from an acne nodule on the face of a negro girl with moderate acne.

Strain P: This was isolated by planting in deep shake tubes of 1 per cent. dextrose agar an emulsion of scales from the seborrheic scalp of the patient from whom Strains A and E were obtained.

Strain R: This was isolated in deep shake tubes of 1 per cent. dextrose agar from the contents of a small nodule on the face of a patient with moderate acne.

Strain S: An effort was made to grow the organism from the diseased tissue of an acne lesion. For this purpose, a raised, hard, dark red nodule was chosen, about 1 by 0.5 cm. in size. This was situated

just beneath the ear on the side of the neck, where there were no visible hairs and no evidence of softening or pus formation. After careful sterilization, the whole nodule was excised and put in a sterile petri dish with the skin side down. The granulomatous tissue was then removed in small pieces with a small curet, carefully avoiding any visible follicle sacs. What appeared to be a distended sac was seen near the center of the lesion. These one-half pinhead-sized bits of tissue were planted aerobically and anaerobically on 1 per cent. glucose agar, 2 per cent. glycerin agar, Fleming's medium and 1 per cent. dextrose agar plus 10 per cent. ascitic fluid. The p_H of these mediums varied from 6.4 to 6.6. One or more pieces were also macerated in salt solution and deep shake tubes inoculated; one series had a p_H of 6.6 and another of 7.8. No growth was obtained except on the anaerobic tubes of the 1 per cent. dextrose agar and Fleming's medium. Both of these tubes, after about two weeks, showed a scanty grayish, thin pure culture of acne bacilli. After several subcultures, however, the organisms gradually assumed a characteristic cultural appearance.

Strain T: This was isolated in deep dextrose agar shake tubes, from an acne papule on the chin of a negro girl.

Strain Y: This was isolated in deep shake tubes from an acne nodule on the neck.

General Technic.—In cultivating the organism aerobically, we found it necessary to transfer large amounts of material. On slants, a straight needle was used; a pinhead-sized mass of the bacteria was planted, and the needle was pushed down through the mediums. A large loopful was also used in inoculating fluid mediums and a little of it was allowed to sink to the bottom of the tube.

When anaerobic methods were used, it was not necessary to employ such large amounts of material, although a thick seeding was desirable to secure good growth. On the various slant mediums, a good sized loopful was thickly smeared over the surface. Thin smears usually resulted in no growth, or the growth would take place only in certain points where the seeding was thickest.

The majority of cultures were rendered anaerobic by the pyrogallic acid-sodium hydrate method, either by the modification described by Wright or by placing the tube or plates in desiccators and quickly adding solutions of the required chemicals. In the former method, after the cotton plug had been pushed down into the tube, pyrogallic acid powder was packed into the top for a depth of from 2 to 3 cm., wet with a 50 per cent. sodium hydrate solution, and a rubber cork quickly applied. In the latter, 1 gm. each of pyrogallic acid and sodium hydrate in solution were used for each 100 c.c. of cubic space.

A good growth was also obtained by placing cultures in desiccators equipped with stopcocks and exhausting the air to one-half atmospheric pressure.

The anaerobic jar described by Brown [15] was used in some instances, but the results, in general, were not so good as with the pyrogallic-sodium hydrate method.

Growth on Various Mediums.—These mediums, when possible, were adjusted between p_H 6.2 and 6.8 unless otherwise stated.

(*a*) Meat Infusion Agar: Anaerobically, moderate growth was obtained, but it was comparatively scanty and did not show the pigmentation seen on more favorable mediums. Some growth was also noted in some of the tubes with aerobic incubation.

(*b*) Meat Infusion Agar Plus 1 Per Cent. Dextrose or 2 Per Cent. Glycerin: These were the most satisfactory mediums for the surface growth of the organism. Many parallel series of cultures did not show the superiority of one over the other. No advantage was found in the addition of 0.1 per cent. oleic acid to the glycerin agar, as recommended by Fleming. On the dextrose or glycerin agar, with anaerobic incubation, growth may be observed in two days, but one or two weeks should be allowed for full development. It may be abundant over the entire inoculated area with a smooth, moist surface; or it may occur in ridges with beadlike projections, here and there, having developed only where the seeding was thickest. It is raised, often luxuriant, and does not spread beyond the margin of inoculation unless transferred by water of condensation. The color varies from a faint pinkish tint to a deep pink or red. The growth is soft, moist, not sticky and is easily emulsified in broth or salt solution. The organism grew well on agar, which had been enriched with ascitic fluid or rabbit's blood, but these mediums were not superior to the 1 per cent. dextrose agar.

When cultivated aerobically, increase in the size of the transplant is usually not apparent before five days or more. As a rule, it will gradually increase in size for three or four weeks. It forms a heaped-up, smooth, round or oval putty-like mass, which may reach 4 mm. in diameter and 2 or 3 mm. in depth. As the cultures grow older, they gradually assume a grayish-brown tint when growth has been good. If growth has been poor, there may be no pigmentation.

(*c*) Extract Agar: Seven strains planted on extract agar both aerobically and anaerobically showed no definite growth. With the addition, however, of 1 per cent. dextrose, out of ten strains planted, one showed a slight growth aerobically and four a scanty growth anaerobically.

15. Brown, J. H.: J. Exper. Med. **33**:677, 1921.

(*d*) Agar Plates: Although the bacilli grew well in 1 per cent. dextrose infusion agar shake tubes, we were unable to obtain satisfactory growth in plates of the same medium or with the addition of 5 per cent. rabbit's blood, incubated anaerobically and aerobically. Fine colonies appeared from some of the strains within the mediums and occasionally on the surface when anaerobic methods were used, but did not usually develop beyond the size of pin points. In one series, however, quite large colonies developed from both strains Y and A in and on the surface of the agar plates. These varied up to 2 mm. in size, and were well pigmented. Two other strains, however, incubated in the same jar showed no growth of one; and only pin-point colonies developed in the other.

The organisms grew well, however, in the inverted petri dishes, as described by Krumwiede and Pratt.

(*e*) Deep Agar Shake Tubes: Growth in 1 per cent. dextrose infusion agar shake tubes is quite characteristic. With thick seeding, the first colonies usually appear after two or more days in a narrow band 1 or more centimeters below the surface of the agar, according to the rapidity of development. This band is sharply defined both above and below and is usually about 0.5 cm. wide. After one or two days, colonies make their appearance in the deeper layers, and usually all the way to the bottom. In some cases, however, a narrow band from 0.25 to 0.5 cm. broad and almost or quite free of growth remains between the upper zone of growth and the deeper colonies. In tubes in which the dilution is higher, this mode of growth is not so striking, but the largest colonies usually appear in the second quarter of the medium measured from the top. In a few instances in which growth was very slow, development of colonies were seen limited entirely to the upper zone, i. e., none appeared in the lower portion of the agar. The colonies vary in size from that of pin points to 2 mm., and when large enough to be well observed with the naked eye are always compound. They usually resemble two convex disks intersecting each other at right angles, but later they may be more complicated in appearance. They are grayish with occasionally a pinkish or brownish tint. We have never seen them develop as a single convex disk, which is the usual appearance of the staphylococci. The colonies of staphylococci never reach the size of the large colonies of the acne bacillus, so that in some of the tubes of the higher dilutions it is usually easy to pick out pure cultures of the latter.

As a rule, the addition of ascitic fluid to the deep agar tubes markedly increased the rapidity of growth of the colonies of the bacillus.

For our deep shake tubes, we used the ordinary infusion agar containing either 1 or 1.5 per cent. of agar.

(*f*) Broth: We used a hormone broth prepared by the method described by Fisk and Burky.[16]

All of our strains grew luxuriantly in either 1 per cent. dextrose or 2 per cent. glycerin hormone broth, when incubated anaerobically. A heavy granular sediment was formed on the bottom of the tubes, which often extended up the sides for some distance. There was no pellicle formation, and the broth was clear with all of our strains, with the exception of strain M, which always produced clouding of the medium. This sedimentary growth often had a pinkish or brownish tint.

In the same mediums under aerobic conditions, growth usually occurred slowly, and then only when the inoculum was large and a small mass had been allowed to settle to the bottom.

In plain hormone broth, growth was obtained both aerobically and anaerobically, but it was inferior to that obtained when sugar or glycerin was present.

(*g*) Milk: In the aerobic series, five strains showed soft curd formation, and in the anaerobic series seven strains showed curd formation with extrusion of whey. The remaining strains, however, showed a layer of curd over the bottom of the tube and coagulated completely on heating. Addition of whey from the cultures to fresh raw milk did not cause coagulation, indicating the lack of a coagulating enzyme.

(*h*) Extract Gelatin: No growth was apparent in any of the tubes after incubation at 20 C. for three weeks. A series of tubes with a p_H 7.8 was planted as well as the series of p_H 6.6. (Infusion gelatin was not tried.)

(*i*) Potato: Five strains were planted on potato both aerobically and anaerobically. After ten days, there was no definite growth on the aerobic tubes, but all the anaerobic tubes showed moderate growth with a deep pinkish color. The growth in general was not so luxuriant as on dextrose agar.

(*j*) Loeffler's Blood Serum and Dorsett's Egg Medium: Both gave good growth anaerobically, but aerobically the results were not so good as on dextrose agar. The pigmentation was darker than on dextrose or glycerin agar. On Loefler's medium, a blackish-blue tint was present.

(*k*) Ground Cooked Meat: Visible growth took place only in the top layers of the meat underneath the supernatant fluid.

CONTAMINATING ORGANISMS

Besides staphylococci, we encountered only one other organism as a contaminant of our original cultures. In only one case did we find a

16. Fisk and Burky: J. Infect. Dis. **30**:128, 1922.

contamination with staphylococci which was not evident in the original by its macroscopic appearance. The other organism found was a bacillus differing entirely morphologically from the acne bacillus, but resembling it in many respects in its cultural characteristics. In thirteen strains isolated as apparently pure cultures of the acne bacilli, this other organism was also found three times.

We first observed it as a contaminant of strain H, which was isolated anaerobically from an acne papule on glycerin agar. A clean, pinkish growth of the usual acne bacillus type occurred. Transfers were made in deep dextrose agar shake tubes, and on the fourth day, in the anaerobic zone, several large colonies were noted which were three or four times as large as the colonies of the acne bacillus. The organism was next encountered in strain L, which was isolated anaerobically on glycerin agar from a seborrheic filament. This strain was grown through several transfers, and nothing unusual was noted until deep tubes were inoculated, and it was then found that practically all the colonies were of the large type. It was found for the third time in strain N, which was obtained aerobically from an acne papule. The culture showed a central pinkish growth surrounded by a mantle of staphylococci. After standing for two or three weeks, a transfer was made from the center anaerobically. This gave a pinkish growth of the usual type. On subcultivating in deep shake tubes, both the acne bacillus and the other bacillus were obtained.

In pure culture, this organism, so far as we have studied it, resembles the acne bacillus in its cultural characteristics. It grows luxuriantly anaerobically on acid glycerin or dextrose agar and aerobically if transplanted en masse. The growth has the same heaped up character as the acne bacillus, but it is dryer. It is pinkish or grayish brown, with usually a metallic luster in old cultures. In deep shake tubes it appeared sooner and the colonies were usually much larger than those of the acne bacillus, occasionally reaching 4 mm. in size.

We have so far noted no tendency for it to show preference for growth in the upper zone of the shake tubes; on the contrary, it grew better in the lower half of the medium. The colonies are usually compound, but single convex ones have been observed. They are often pigmented and at one time a deep red color was noted.

Microscopically, the organism is a bacillus from 1 to 2 microns in length by 0.5 to 0.8 microns in width. It occurs singly, in pairs or less frequently in short chains. The ends are rounded, and frequently the cell is thicker at one end than the other, so that it has a wedge shape. In many cases, Gram's stain is retained irregularly, and the cell appears to contain one or more deeply stained granules. Degenerating forms appear rapidly as the culture grows older. These are characteristic, and con-

stitute its chief morphologic difference from the acne bacillus. The degenerating cells are usually considerably thicker than the younger forms, although there is a great deal of variation in size. The most common form is an oval or ovoid cell, with a deeply staining granule in one end and the rest of the structure staining faintly or showing only in outline. Occasionally, the cell may be round, with one or more irregular granules around the border; or elongated forms may be present with the granule near or in the center. Small clumps of cells were at times encountered which were very much smaller than the young forms. They had a columnar shape with a granule in the center or toward one end, which gave them the appearance of columnar epithelial cells. We were unable to obtain a positive spore stain. In some of our old cultures, practically all of the cells were of the degenerating type.

Cultures of this organism appear to die out much more quickly than those of the acne bacillus.

COMMENT

We have been able to isolate and cultivate the acne bacillus by both aerobic and anaerobic methods without difficulty, after we had determined the hydrogen-ion concentration of the mediums suitable for its best development. Ten strains from various sources showed no essential difference microscopically or in their cultural characteristics. The organism grew well on meat infusion agar, to which 1 per cent. dextrose or 2 per cent. glycerin had been added. Moderate growth took place on plain meat infusion agar anaerobically, and occasionally slight growth aerobically, but results were practically negative on plain extract agar. It is essential that the p_H of the mediums shall be acid, preferably somewhere between 6.2 and 6.8. We believe that the use of mediums with the wrong acidity has been responsible for most of the difficulties previously encountered in cultivating the organism.

Under the most favorable conditions the bacillus grows slowly but usually luxuriantly. It has a strong communistic tendency; unusually large amounts of inoculum are necessary for successful transplantation.

The formation of pigment is a characteristic trait of the organism when grown under favorable conditions. Sabouraud mentions the brown or rose color of the growth, and Gilchrist says that old cultures acquire a mahogany or almost black color. Fleming also speaks of the colonies becoming almost black when old. Of those using anaerobic methods of cultivation, color formation is mentioned by Lovejoy and Hastings.

All of our strains were pigment producers. When grown aerobically, a grayish-brown tint usually developed as the culture grew older. If the growth was poor, no color resulted. With anaerobic cultivation, the color varied from a faint pinkish tint to a deep pink or occasionally a

deep coral red, although sometimes a good growth was obtained with little pigmentation. We have frequently seen two or three shades of color in one culture where several separate colonies had arisen from a mass of pus or a filament. After anaerobic tubes are opened, the pinkish or red color is quickly lost, giving place to the dark brown tint characteristic of old aerobic cultures.

The production of pigment occurred on all the different solid cultural mediums used where growth was good, and there was often a pinkish or reddish tint to the sediment of broth cultures. The pigment was insoluble in water, chloroform and ether.

The acne bacillus, although it grows best under anaerobic conditions, is not a strict anaerobe, as shown by its preference for the upper zones of deep shake tubes where a small amount of oxygen is present and by the fact that it can be grown aerobically when transplanted en masse. In the latter case, however, we are, undoubtedly, dealing with partial anaerobic conditions, growth taking place, as has been expressed by Lovejoy and Hastings, by inner tumefaction rather than by lateral extension. One of our experiments is also suggestive that the organism requires some oxygen for its growth. Ten strains were planted on 1 per cent. dextrose agar in duplicate series. One set was prepared by the Wright method for producing anaerobiosis. The other set was put in a Brown jar and the air exhausted until the medium was pulled up from the bottom of some of the tubes. The jar was then connected with the hydrogen tank and the electric current run through for one hour. The latter process was repeated again on the following day. After five days' incubation, the tubes made anaerobic by the Wright method showed a luxuriant pigmented growth. In the other series of tubes, however, incubated in the Brown jar, only a thin, poor noncharacteristic growth occurred.

The morphology of the organism has often been described by other investigators. Sabouraud says that it is encapsulated, but we were unable to demonstrate a definite capsule, although in some cases an interbacillary material seemed to be present. Involution forms were present in old cultures, and organisms resembling the branching forms described by Gilchrist were encountered; but whether these represent a true or false branching, we have so far not been able to determine.

We are not yet prepared to discuss the significance of the bacillus which was found in three of our cultures of the acne bacillus. Although it has some resemblance to the bottle bacillus, our investigations with it have not progressed far enough to justify the expression of a definite opinion. Further work with the organism is in progress.

CONCLUSIONS

1. The acne bacillus grows best in an acid medium with a hydrogen-ion concentration between 6.2 and 6.8.

2. It is a slowly growing organism, which shows its best development under anaerobic conditions, but which will grow under aerobic conditions if transplanted en masse.

3. The addition of some enriching substance, such as dextrose or glycerin, to agar or broth is necessary to obtain good growth.

4. Pigment formation is a characteristic trait when the organism is grown under favorable circumstances.

5. We have described an unidentified bacillus, present in three out of thirteen supposedly pure cultures of the acne bacillus. So far as our investigations have gone, this organism resembles, in many respects, the acne bacillus in its cultural characteristics. Morphologically, its chief characteristic is its curious degeneration forms.

DERMATITIS GANGRENOSA INFANTUM *

REPORT OF A CASE

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In reviewing the literature on this comparatively rare disease, first definitely described as a clinical entity by Hutchinson [1] and Stokes,[2] we found that it was at first thought to follow vaccination and vericella. But later writers and investigators, Crocker,[3] Elliot,[4] Zuber,[5] and others found cases that were definitely of primary origin.

In the cases of primary origin, the patient was usually an ill nourished child under 3 years of age. The lesion started as a papule, becoming a bleb, then a pustule and developing into an ulcer covered by a scab. This when removed left a crater with perpendicular edges and a flat base, usually penetrating all layers of the skin. The gangrenous ulcers were usually situated about the buttocks and thighs.

The cases following varicella, vaccinia or other pustular conditions of the skin were usually situated about the head and trunk, the course of the disease being the same as in those of primary origin, except that the patients were not always of the poorly nourished variety.

The etiology of the disease has not been definitely worked out. Boudouin and Wickham [6] found *Streptococcus pyogenes,* but were not sure of the pathogenic importance. Hitschmann, Kreibich,[7] and Ehlers [8] found *Bacillus pyocyaneus* predominating, while others thought *Bacillus diphtheriae* the causative organism.

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* Read before the St. Louis Pediatric Society, June 5, 1924.

1. Hutchinson: Gangrenous Eruption in Connection with Vaccination and Chickenpox, Lond. Med. Chir. Tr., 1882; Rare Diseases of the Skin.

2. Stokes: A Case of Vaccinia Gangrenosa, Dublin J. M. Sc., June, 1880.

3. Crocker: Multiple Gangrene of the Skin in Infants and Its Causes, London M.-Surg. Soc. Tr., 1887 p. 397.

4. Elliot: Dermatitis Gangrenosa Infantum, M. Rec. May 16, 1891, p. 562.

5. Zuber: Disseminated Gangrene in the Skin in Infants, La Clin. Infantile **12**:388 (July 1) 1914.

6. Boudouin and Wickham: Ecthyma terebrant des enfants, Ann. de dermat. et syph., 1888.

7. Hitschmann, Fritz, and Kreibich: Pathogenese des Bacillen Pyocyaneus und zur Aetiologie des Ecthyma Gangrenosum, Wien. klin. Wchnschr., 1897, No. 50. Ein weiterer Beitrag zur Aetiologie des Ecthyma Gangrenosum, Arch. Dermat. u. Syph. **1**:81, 1899.

8. Ehlers: Deux cas d'ecthyma terebrant des enfants, Ann. de dermat. et syph., 1891, p. 93.

The treatment consisted of building the child up generally with tonics and stimulants and plenty of nourishing food. The local treatment consisted of the application of antiseptics, such as 5 to 10 per cent. ointment of sulpho-ichthyolate preparation, saturated solution of boric acid with from 2 to 5 grains (0.15 to 0.32 gm.) of resorcin to the ounce, mercuric chlorid 1:2,000 to 1:5,000 as a wash. Thymol iodid or boric powder was dusted on following the application of one of the lotions referred to in the foregoing.

The prognosis in the debilitated infants was generally bad. In those over 1 year of age, when the condition was secondary to some pustular disease, the prognosis was better. Many cases of recovery were reported.

REPORT OF A CASE

History.—Edward A., a colored boy, aged 14 months, was sent to the isolation hospital on April 23, 1924, with complaint of cough, suspicious whooping, labored, frequent respirations, sore mouth and eye and nasal and aural discharges. He had entered the hospital for colored people three days previouly, with a history of having contracted measles two weeks before, and during a late stage of convalescence, he had developed a cough, cold in the head with sore mouth and eye, and a high fever. He was an inmate at an orphanage so that the past and family history could not be obtained.

Examination.—The entrance examination revealed an undernourished and poorly developed infant, conscious, but acutely ill. The temperature was 105 F., the pulse rate 150 and the pulse was of small volume and easily compressible. Respiration was rapid (60 a minute) and labored, with dilatation of the ala nasae. The conjunctiva of the right eye was reddened and edematous, and there was a purulent exudate coming from the inner canthus. Purulent discharges were also present in the nostrils and the right ear. On the upper lip were three round crater-like ulcers, deeply excavated, with slightly undermined edges. The bases of these ulcers were necrotic and covered with a seropurulent exudate. Crusting was present in the corners of the mouth. The teeth were in a fair condition; the tongue was coated grayish white; the tonsils were enlarged, and the throat was hyperemic. There were no abnormalities of the thymus or thyroid glands, but the anterior and posterior cervical lymph nodes were enlarged.

The thorax was of the pigeon breast type, and there was prominent costochondral beading. Diminished resonance, with bronchovesicular breathing and moist râles were general over the fields of both lungs. Pleural friction rubs were both palpable and audible in the axillary line on both sides—more prominent on the left. The abdomen was grossly normal. The liver and spleen were not palpable.

An ulcer, about 1.5 cm. in diameter, was present on the ventral surface of the right forearm. The edges of this ulcer were perpendicular, and the base was covered with a seropurulent discharge. There was a dark red areola extending for a short distance around the ulcer.

Laboratory Findings.—Laboratory examination revaled: red blood cells, 3,600,000; white blood cells, 26,000; polymorphonuclear neutrophils, 90 per cent.; hemoglobin, 70 per cent.; blood pressure: systolic, 90; diastolic, 60. The Wassermann test was negative. Cultures of the throat were negative for

diphtheria. Cultures of the nasal discharge contained staphylococci. Cultures of the ear discharge contained staphylococci and streptococci. Blood cultures showed no growth.

The patient was treated for bronchopneumonia and whooping cough. A slight improvement of the chest condition was noticeable in a few days. The temperature descended from 105 to 102 F. The pulse rate decreased and the respirations became less rapid and labored. However, within a few weeks, the ulcer on the wrist had doubled in size, and a new lesion appeared a short distance up the arm, forming a papule first, then progressing through the vesicular and pustular stages. Cultures and smears were obtained from the new lesion before it ruptured spontaneously, but the contents proved to be sterile. The ulcerations on the lip likewise continued to progress, and the corners of the mouth and inner canthus of the right eye sloughed out.

The case was seen by several dermatologists and pediatricians, and various diagnoses were made and treatments instituted for the skin condition. The diagnoses of syphilis, noma and a tuberculid were not borne out by clinical appearance, course or therapeutic reaction. Repeated Wassermann tests were negative. Smears made from the ulcerating areas showed *Streptococcus pyogenes* and *Staphylococcus aureus.*

The ulcerations progressed in spite of local applications of mercurochrome, gentian violet and arsphenamin in glycerin. Mercurial inunctions and arsphenamin intravenously failed to produce a favorable reaction. Three weeks after admission a diagnosis of dermatitis gangrenosa infantum was made, and local applications of 1 per cent. resorcin in saturated solution of boric acid, followed by a dusting powder of thymol iodid, were instituted four times daily. This produced an immediate improvement. Within a week the lesions about the mouth, lips, nose and eye had almost healed, and the lesion on the wrist had decreased in size by one-half.

The condition of the lung apparently remained stationary. The râles disappeared, but the bronchovesicular breathing on the left side indicated an unresolved pneumonia, or abscess formation, and the pleural friction rubs were still present on both sides. Pus was obtained on puncture. The temperature ranged from 99 to 103 F. The pulse rate was 156; respirations, 42. The Wassermann test again was negative; and the blood pressure was: systolic, 82; diastolic, 50.

Two weeks after the child was admitted, a child in a neighboring bed developed chickenpox. About a week and a half after the primary lesions had nearly healed, a new crop of lesions began to appear at various sites over the whole body, mostly over the back and extremities. These started as small papules, then became vesicular and pustular, and the condition was diagnosed a true varicella. However, instead of crusting, healing and scaling, a number of these lesions showed a tendency to follow the same course of ulceration and necrosis as the former lesions. One over the left tibia gained a diameter of 1.5 cm. Several on the anterior thorax and right side of the face were 1 cm. in diameter. These all showed little improvement with the foregoing treatment.

On June 5, the forty-fourth day in the hospital, the child became cyanotic, had great respiratory difficulty, vomiting and a profuse diarrhea. The chest findings were the same as previously described, but exaggerated. The pulse was rapid and thready. The heart was enlarged to the right and left to percussion. He died at 5 p. m.

COMMENT

This case was apparently one of primary origin when the patient first entered the hospital, but the later series of gangrenous ulcerations were secondary to the varicella that the patient had contracted from his neighbor in the ward.

Apparently the causative organism in this disease, as stated by Zuber, depends on the organisms found on the skin at the time the child develops the pustular disease. In this case, the resistance of the tissues to the invasion of the ordinary pyogenic organisms was reduced by the series of infections (measles, pertussis with bronchopneumonia and varicella) combined with the general state of malnutrition and rickets.

The pathologic condition in the respiratory system was probably that of pyemia, as shown by similar cases in which necropsy was obtained. It was responsible for the fatal termination (Howard [9] and Crocker [3]).

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9. Howard: A Case of Gangrenous Varicella, Brit. M. J. **1**:904 (May) 1883.

Abstracts from Current Literature

Syphilis as the Cause of Muscular Atrophy of Spinal Origin. A. J. Ostheimer, George Wilson and W. W. Winkelman, Am. J. M. Sc. **168**: 835 (June) 1924.

The amyotrophic form of spinal syphilis is considered by the witers as a syndrome due to syphilis of the anterior horns, and may or may not be associated with tabes or paresis. A few cases are reported in support of their contention, but they state that their object is to attract attention to the subject of spinal progressive muscular atrophy, and, when syphilis is found to be the cause, to institute antisyphilitic treatment at once.

The Clinical Value of the Serum Tetrachlorphenolphthalein Test for Liver Function. R. Ottenberg, S. Rosenfeld and L. Goldsmith, Arch. Int. Med. **34**:206 (Aug.) 1924.

In 103 cases, this method was of value in discovering the index of liver function. It is, however, valueless in obstructive jaundice. In a number of cases, it was possible to detect liver disease and in others likewise to exclude it, no false positive results being noted. In three cases of hepatic syphilis in adults, the test was a failure.

A positive test means a serious disability of the liver, 5 per cent. of the dye in the hour serum being regarded as suspicious, 8 per cent. as conclusive, while a negative result does not always exclude the possibility of serious lesions of the liver.

Jamieson, Detroit.

Pulmonary Syphilis. John B. Hawes, 2d, Boston M. & S. J. **190**:92 (Jan. 17) 1924.

A case of pulmonary syphilis is reported, and the following criteria for the diagnosis of such cases are given: Given a patient with a definite syphilitic history, a positive Wassermann reaction, signs of syphilis elsewhere, who has in his lungs, as shown by the roentgen ray and clinical examinations, evidence of an extensive destructive process, especially at the hilum or base rather than at the apex, with sputum constantly negative to tuberculosis, pulmonary syphilis is probable. If the process under antisyphilitic treatment clears up rapidly, the diagnosis of pulmonary syphilis may be considered definite.

Metabolism Observations in Scleroderma. Allan W. Rowe and Francis H. McCrudden, Boston M. & S. J. **190**:121 (Jan. 24) 1924.

A case of extensive scleroderma is reported in which accurate laboratory investigations were made, and in which much stress is laid on the secondary changes occurring in joints, bones and muscles.

Treatment of Late Syphilis. George A. Dix, Boston M. & S. J. **190**:742 (May 1) 1924.

This is a discussion on the therapeutics of late stages of syphilis.

DRUG ERUPTIONS. C. GUY LANE, Boston M. & S. J. **190**:880 (May 22) 1924.

This is a report of eruptions on the skin produced by some of the newer drugs, with a review of recent literature on mechanism of their action.

LANE, Boston.

TREATMENT OF PRURITUS ANI, VULVAE AND SCROTI. M. P. MOORER, J. A. M. A. **83**:766 (Sept. 6) 1924.

The author recommends infiltration of the perianal tissues with a 0.25 to 0.5 per cent. solution of quinin and urea hydrochlorid. The anesthesia thus produced lasts for several days or weeks, and during this time the effects of scratching subside and the causative factor can be searched for. A second or third infiltration may be required.

THE USE OF TRYPARSAMIDE IN THE TREATMENT OF GENERAL PARALYSIS: RESULTS OF FIRST YEAR'S EXPERIENCE. F. G. EBAUGH and R. W. DICKSON, J. A. M. A. **83**:803 (Sept. 13) 1924.

This report, from the psychopathic wards of the Philadelphia General Hospital, comprises fifty-two cases of general paralysis. These cases fall into three groups: (1) the organic group consisting of parenchymatous types with destruction of the central nervous system that has preceded beyond repair, (2) organic reactions with psychoses of functional coloring and (3) transitory psychoses without signs of deterioration.

In Group 1 there were eleven patients, none of whom was influenced. Group 2 comprised thirty-six patients, in ten of whom improvement occurred. In Group 3 there were five patients, all of whom improved. Treatment consisted of ten weekly tryparsamide injections of 3 gm. each. A rest period of eight weeks was given between courses.

Untoward reactions consisted of jaundice (two cases), dermatitis (one case), visual disturbances (one serious case), and neurorelapses (two severe, several mild cases). Because of optic changes, 30 per cent. of the possible candidates for tryparsamide therapy were rejected.

The authors are favorably impressed with the value of tryparsamide in general paralysis. Of fifty-two patients treated, they were able to discharge fifteen who are now self-supporting. The previous year, with older methods of treatment, only five patients were discharged in good condition.

NEUROSYPHILIS SIX OR MORE YEARS AFTER TREATMENT. LOYD THOMPSON, J. A. M. A. **83**:807 (Sept. 13) 1924.

The report deals with fifty-three cases of neurosyphilis. the patients being first seen and treated during the years 1914 to 1917. Treatment in all cases was intensive, consisting of intraspinal and intravenous arsphenamin and mercury, usually intramuscularly.

Of the fifty-three patients, twenty are still living, eight being clinically and serologically well and three clinically well. Of those dead, twenty-two died of neurosyphilis, and eleven of other causes. The best results were obtained in cases of meningitis, the poorest in general paralysis and taboparalysis. The tabes patients who were seen fairly early in the course of the disease, and who received the greatest amount of treatment, responded encouragingly.

TRYPARSAMIDE TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM: OBSERVATIONS FROM AN OPHTHALMOLOGIC STANDPOINT. W. I. LILLIE, J. A. M. A. **83**:809 (Sept. 13) 1924.

Lillie studied the ocular manifestations in 114 cases of neurosyphilis, in order to ascertain the effects on the optic tract of tryparsamide therapy. His conclusions are as follows:

1. Changes in vision, fundi and perimetric fields are much greater in cases of untreated syphilis of the central nervous system than in treated cases.

2. Pupillary and reflex changes are practically the same in treated and untreated cases of syphilis of the central nervous system.

3. Ocular changes occurred as often with arsphenamin treatment as with tryparsamide treatment.

4. The use of tryparsamide is not contraindicated by pathologic changes in the fundus.

5. The arsenicals are apparently efficient in decreasing ocular changes in syphilis of the central nervous system.

6. In this select series of cases, tryparsamide was not more harmful to the eyes than any form of arsenic used in the treatment of syphilis of the central nervous system.

THE MANAGEMENT OF IMPETIGO CONTAGIOSA IN MATERNITY HOSPITALS. J. H. BLAISDELL, J. A. M. A. **83**:833 (Sept. 13) 1924.

Blaisdell calls attention to the seriousness of epidemics of impetigo contagiosa among infants, the death rate in some instances reaching from 25 to 50 per cent. The disease spreads with great rapidity in institutions, and unless the most stringent measures are put into effect cannot be successfully controlled. Infected children and suspects must be segregated, and all infected material sterilized. The cooperation of the nursing personnel is absolutely essential. Sometimes it becomes necessary to close the ward temporarily.

THE RESULTS OF TRYPARSAMIDE THERAPY IN NEUROSYPHILIS. J. E. MOORE, H. M. ROBINSON and S. LYMAN, J. A. M. A. **83**:888 (Sept. 20) 1924.

The authors present the results in treatment with tryparsamide in 195 cases observed during the last four years, of which there were 132 cases of neurosyphilis.

In fifty-two cases of cutaneous and visceral syphilis, the therapeutic response to tryparsamide was so slight that it was negligible.

The authors estimate of the clinical effect of tryparsamide is based on the results obtained in seventy-eight neurosyphilitic patients, of whom twenty-nine had not been previously treated, and forty-nine had received prior treatment without complete relief of symptoms.

There were thirty-six patients with general paralysis, of whom nine had complete remission of all mental symptoms and ten showed distinct improvement. In eighteen patients with tabes, six were completely relieved of lightning pains and gastric crises, and three were improved. The most striking clinical improvement was noted in the meningovascular group, in which all except four were improved or completely relieved.

Tryparsamide seems to be superior to other remedies so far as the relief of clinical symptoms are concerned. Advanced general paralysis is uninfluenced by it.

The effect of tryparsamide on the blood Wassermann reaction is negligible. Its effect on the spinal fluid serology is greater than that of any other arsenical.

Visceral disturbances from tryparsamide occurred in 17.8 per cent. of a series of 241 cases; but in only 2.8 per cent. were they of serious import. Ocular disturbances usually occur early in the course of treatment. They may be obviated to a great extent by careful ophthalmologic control.

A Comparison of Tryparsamide and Other Drugs in Treatment of Neurosyphilis. H. C. Solomon and H. R. Viets, J. A. M. A. **83**:891 (Sept. 20) 1924.

The authors have treated more than 100 neurosyphilitic patients with tryparsamide. Their experience, of only eleven months' duration, does not allow any definite statements in regard to a final evaluation of tryparsamide. Previous reports have recorded remarkable clinical results with the drug, which, on the whole, Solomon and Viets cannot entirely corroborate. They recognize that the interpretation of clinical effects rests to some degree on the personal equation of the clinician and cannot be reduced to a definite mathematical formula. Again neurosyphilis presents so many vagaries in its course that a comparatively short period of observation does not allow definite critical interpretation.

In meningovascular types of neurosyphilis, tryparsamide in their hands, has proved of value, but hardly more so than other arsenicals used by accepted methods.

The authors had no outstanding or brilliant results in tabes or general paralysis. In these diseases, the superiority of tryparsamide over other methods was not demonstrated.

In regard to the serologic effects, the authors found that tryparsamide was more effective in lowering the cell count than was arsphenamin or subarachnoid injections. Likewise, in the reduction of protein an effect superior to other methods was demonstrable. But the colloidal gold curve and the Wassermann reaction were rarely changed to any appreciable degree.

In three patients, a permanent impairment of vision resulted from tryparsamide therapy.

A Case of Multiple Cutaneous Leiomyoma. K. P. Frost, J. A. M. A. **83**: 906 (Sept. 20) 1924.

Frost could find only thirty-nine cases of this condition in the available literature. Two of these are of doubtful character. The author's patient was a woman, aged 28, who complained of a painful skin disease of eight years' standing. The disease began with paroxysmal pain in the back which gradually increased in severity. In the painful area, the skin was thickened and studded with small soft masses slightly darker than the surrounding skin. There were some scattered pink shiny tumors which were painful to the touch. There were some thickened patches without tumor formation on the right upper extremity. Microscopic examination revealed that the tumors were composed of interlaced bundles of smooth muscle fiber.

Treatment with roentgen ray and ultraviolet was without effect.

Eczematoid Ringworm. H. H. Hazen, J. A. M. A. **83**:1123 (Oct. 11) 1924.

Hazen gives a general survey of this subject, with emphasis on its most important phases. In his own practice, the condition occurs in about 10 per cent.

of all patients seen. Apparently it is more common in the South than elsewhere in this country.

Disability from the disease varies from 2 to 10 per cent., according to replies to a questionnaire sent to leading dermatologists throughout the country. In the author's practice, it was over 30 per cent.

Hazen does not believe that pompholyx exists; in every case seen in his office with the clinical picture of pompholyx, study has shown fungi present. Some cases are nearly intractable to treatment, and recurrences are frequent. Whitfield's ointment, which should be much stronger in salicylic acid than originally prescribed, and mercurochrome-220 soluble have proved of great value. The roentgen ray is often useful.

There are many phases of this subject which urgently demand serious study. The disease is of such importance that an epidemiologic study is urgently needed. Better methods of treatment are likewise required.

ACCIDENTAL MALARIAL INFECTION IN SYPHILIS OF THE BRAIN. L. E. HINES, J. A. M. A. **83**:1161 (Oct. 11) 1924.

A patient from the tropics developed severe general symptoms, including fever and coma. The blood contained malarial parasites; the Wassermann reaction of the spinal fluid was strongly positive. The patient died, and necropsy revealed diffuse malarial thrombosis of the capillaries of the brain and chronic syphilitic leptomeningitis. The anatomic findings were those that might be produced by syphilis and malaria together, and there was no anatomic evidence that the syphilitic lesions were changed by the malarial infection.

The case is recorded because of reports in the foreign literature of the treatment of general paralysis by induced malarial infection.

GANGRENE OF FINGER DUE TO SCLERODERMA. J. GOTTESMAN, J. A. M. A. **83**:1162 (Oct. 11) 1924.

In a case of scleroderma involving both the hands and feet, gangrene of one finger developed, and necessitated amputation. While trophic disturbances and superficial necroses are common in this disease, actual gangrene appears to be rare.

INDIA INK IN THE MICROSCOPIC STUDY OF YEAST CELLS. F. D. WEIDMAN and W. FREEMAN, J. A. M. A. **83**:1163 (Oct. 11) 1924.

The authors recommend the use of the India ink method for demonstrating the mucinoid coating of yeast cells.

A CASE OF MYCETOMA. L. C. AUDRAIN, J. A. M. A. **83**:1165 (Oct. 11) 1924

The author reports a case of mycetoma in a youth, aged 18, in otherwise excellent health. This patient was given six injections of neo-arsphenamin without effect. Then mercurochrome-220 soluble intravenously alternating weekly with neo-arsphenamin was administered. In all, eighteen injections of each drug were given.

The patient was cured. The report of this case is simply a suggestion, with the hope that this combination may prove successful in other cases, and thus do away with the necessity of amputation in this disease.

TUBERCULOSIS OF THE TONGUE. H. MORROW and H. E. MILLER, J. A. M. A. **83**:1483 (Nov. 8) 1924.

This condition has escaped mention in dermatologic textbooks, though the authors believe that its importance from a diagnostic standpoint warrants the attention of dermatologists. The condition is probably not as rare as the literature would lead one to judge. The authors record sixteen cases, one primary, the others secondary. The incidence of the condition was 1 per cent. in cases seen in the tuberculosis service of San Francisco Hospital. Clinically, the disease appears as nodular, ulcerative and papillomatous types. The differential diagnosis is discussed. The majority of cases require pathologic investigation to differentiate them from other conditions.

The best local treatment was surgical removal of the solitary lesions. The cautery may be of some value in extensive ulcerating lesions.

THE PROPHYLAXIS OF ROENTGEN-RAY OVERDOSAGE. R. H. RULISON, J. A. M. A. **83**:1505 (Nov. 8) 1924.

Through the omission of a filter, Rulison's patient received 4⅓ skin units to a senile keratosis in the face. This area was then given seven Kromayer light exposures during a period of two weeks. There was no untoward effect from the excessive roentgen-ray dose, and the author believes that this can be attributed to the Kromayer light treatment.

THE ACTION OF BURIED GLASS CAPILLARIES OF RADIUM EMANATION ON PLANT AND ANIMAL TISSUES. I. LEVIN and M. LEVINE, J. A. M. A. **83**:1645 (Nov. 22) 1924.

The authors have studied the effect of buried glass capillary tubes of radium emanation. Their effect on crown gall and other tumors of plants, sarcoma and carcinoma of mice, as well as clinical experience on human tumors, lead to the conclusion that the intratumoral insertion of bare capillary glass tubes of radium emanation presents today the best single method of radiotherapy in various types of carcinoma and sarcoma for the following reasons:

1. It allows an even distribution of small quantities of radiations throughout the tumor.

2. On account of the intimate contact of the radio-active substance with the tumor cells, the total amounts are small and local results are obtained without any general effect on the organism.

3. Use is made of the beta rays, which do not act as a simple caustic agent but destroy the nearest cancer cells and at the same time create secondary gamma rays, which affect malignant cells at a distance in the same manner as gamma rays of radium and roentgen rays.

MICHAEL, Houston, Texas.

FURTHER OBSERVATIONS ON THE PHENOMENA ENCOUNTERED IN ATTEMPTING TO TRANSMIT VARICELLA TO RABBITS. T. M. RIVERS and W. S. TILLETT, J. Exper. Med. **39**:777 (June) 1924.

In the course of this investigation, a hitherto unknown filterable virus, called Virus III, was inoculated intradermally with better results than when smeared on scarifications, giving immunity for at least six months, whether the inoculation was intradermal, intratesticular, intracerebral or intranasal.

Heated virus did not produce visible skin reactions or demonstrable immunity. No passive immunity to this virus could be demonstrated if intravenous injections of immune rabbit serum had been given twenty-four hours previously, or if serum or whole blood of convalescent varicella patients had been given.

An intradermal inoculation of Virus III in a person who had never had varicella produced practically no local or general reaction, while one who had had varicella suffered a moderate general and local reaction.

The authors conclude, however, that their investigations have not proved that Virus III bears any etiologic relationship to varicella.

OBSERVATIONS ON THE PRESENCE OF A TOXIC SUBSTANCE IN THE BLOOD AND URINE OF PATIENTS WITH SCARLET FEVER. J. D. TRASK, JR., and F. G. BLAKE, J. Exper. Med. **40**:381 (Sept.) 1924.

Intracutaneous injections of blood serum, obtained from patients acutely ill with scarlet fever, have demonstrated the presence of a toxic substance when injected into persons who have not had scarlet fever and whose serums failed to blanch the scarlatinal erythema. The reaction produced was a bright red local erythema lasting from one to four days, control injections being negative in persons whose serums blanched the scarlet fever rash. This toxic substance was neutralized by mixture with a positive blanching serum and by Dochez's scarlatinal antistreptococcic serum, but was not neutralized by a negative one nor by horse serum.

A similar toxic substance was found in the urine of two of the patients studied.

The authors believe that their experiments support the conception that scarlet fever is a local infection of the throat of a particular type of *Streptococcus hemolyticus* capable of producing a toxin which is absorbed and is the cause of the general manifestations of the disease.

SYPHILIS OF THE BLADDER. A. PETERSON, J. Urol. **12**:59 (July) 1924.

This is a report of two cases of syphilis of the bladder, calling attention to the fact that earlier lesions are most frequently at the ureteral openings, the later lesions being ulcerating gummas with the possibility of fistulas developing.

SYPHILIS OF THE EPIDIDYMIS. H. C. ROLNICK, J. Urol. **12**:147 (Aug.) 1924.

The writer believes that syphilitic epididymitis is more frequent than is generally believed, as it commonly occurs early in the disease, is usually painless and generally secondary to a syphilitic orchitis, although it may be primary.

He reports four cases, one of which he thinks was of the primary type.

JAMIESON, Detroit.

THE PHYSICAL AND PATHOLOGICAL CONDITIONS GOVERNING THE PATTERN AND DISTRIBUTION OF CUTANEOUS REACTIONS. H. G. ADAMSON, Brit. J. Dermat. & Syph. **36**:1, 1924.

This is an interesting article which does not lend itself readily for abstracting.

It covers the influence of external agents in the determination of the distribution of eruptions, the partiality of certain micro-organisms for particular sites or soils as a determining factor, the influence of the nervous system on

the distribution of skin affections, the distribution of affections of embryonic origin, and the influence of blood vessel distribution in determining the distribution and pattern of certain skin eruptions.

SOME REMARKS ON THE HISTORY OF THE DISCOVERY OF THE ACARUS SCABIEI. C. G. CUMSTON, Brit. J. Dermat. & Syph. **36**:13, 1924.

A brief historical article showing that *Acarus scabici* was first discovered by Dr. J. C. Bonomo, of Leghorn, Italy, in 1687; that the itch was clinically known and its treatment by sulphur ointment current in the middle of the eighteenth century.

A CASE OF ARGYRIA. DOUGLAS FIRTH and G. A. HARRISON, Brit. J. Dermat. & Syph. **36**:105, 1924.

The authors report an extensive case of argyria occurring in a man 63 years of age, who had been applying silver nitrate to the tongue daily for from sixteen to twenty years. As a result of the examination, the authors state that the silver is first deposited in the sweat glands and not until later around the elastic fibers which lie below the epidermis. They suggest that this point may be of practical importance in establishing a diagnosis in early cases, as in the current textbooks examined, with but a single exception, the early deposit in the sweat glands was not noted. They recall that Maranon points out that the pathogenesis of argyria may depend on an unknown factor, since the condition should be more common than it is if argyria depends solely on the amount of silver administered. He suggests that it is possible that the silver, in a soluble form, is dispersed generally throughout the circulation, but it may be that it is only in the sites mentioned above that chemical conditions exist for its precipitation and subsequent reduction.

TREATMENT OF XANTHELASMA PALPEBRALE WITH CONCENTRATED CARBON ARC LIGHT (FINSEN). SVEND LOMHOLT, Brit. J. Dermat. & Syph. **36**:112, 1924.

Lomholt states that the Finsen light has been used with success and with a considerable degree of certainty in the removal of xantoma lesions in twenty cases. The light is applied in the same manner and in the same doses, two hours irradiation daily, as in the Finsen treatment of lupus vulgaris.

A total application of from four to six hours will usually suffice in the ordinary flat form.

MACULAR ERYTHEMA IN A PATIENT WITH A TRAUMATIC HAEMATOMA IN THE ABDOMEN. C. RASCH, Brit. J. Dermat. & Syph. **36**:157, 1924.

Rasch describes a macular erythema in a man, aged 19, following an injury to the abdomen, which produced a swelling presumed to be a hematoma. The patient was a "bleeder." The eruption closely resembled syphilis, but the latter was excluded in the diagnosis. The author suggests in view of Whitfield's article, published in the Lancet in 1921, that the resorption of blood and torn muscle tissue may be looked on as the possible cause of the erythema. As an alternative suggestion, he calls attention to the possibility that bacteria circulating in the blood may have produced changes in the hematoma, which though not of sufficient intensity to give rise to fever or abscess formation, may have occasioned the erythema through toxin formation or in some other manner.

REPORT ON BAKERS' DERMATITIS. ALLAN C. PARSONS, Brit. J. Dermat. & Syph. **36**:193, 1924.

Parsons reviews the subject of bakers' dermatitis and finds that manual contact with dough is a fundamental factor in its etiology. Personal habits and personal predisposition also play a part. Inferiority and adulteration of war flour may have been incidental factors, but there is no proof that the refining processes used at present by flour millers have any particular connection with dermatitis among bakers. The handling of sugars, salt, cream powders and acid phosphate of lime, are other factors which may play a part.

He concludes that it seems probable that the majority of true cases of bakers' dermatitis are caused by the chronic irritation of dough. In prophylaxis the use of machine, rather than hand mixing of dough, improved toilet facilities and the thorough cleansing and drying of the arms after the operation of dough mixing are all important.

HYPERTROPHY OF THE MALE NIPPLE IN LEPROSY. A. POWELL, Brit. J. Dermat. & Syph. **36**:203, 1924.

Powell called attention to hypertrophy of the male nipple as a common but hitherto undescribed sign in male lepers in 1917. Since that date he has examined sixty-seven Indian lepers and has found both nipples enlarged in thirty-three and the left nipple only enlarged in one. In females with leprosy he gathered the impression that the nipples are smaller than in those of healthy females, probably due to the absence of sexual desire and practice in the majority.

A NEW MEDIUM FOR THE GROWTH AND DIFFERENTIATION OF THE DERMATOPHYTES. W. N. GOLDSCHMIDT, Brit. J. Dermat. & Syph. **36**:204, 1924.

Goldschmidt describes a formula for a suitable medium devised to replace that in which maltose "brute de chanut," no longer obtainable, was used.

SENEAR, Chicago.

TREATMENT OF SEVERE EARLY SYPHILITIC RECURRENCES BY A SUPERADDED INFECTION. J. E. R. MCDONAGH, Proc. Roy. Soc. Med. **17**:70 (July) 1924.

The author presented two male syphilitic patients, who were not only resistant to therapy but actually developed gumma while receiving active specific medication. They were inoculated with malaria, and after three weeks of rigors given sufficient quinin to cure. Specific therapy then administered was promptly efficacious.

A CASE OF FOLLICULITIS DECALVANS ET ATROPHICANS. E. G. GRAHAM LITTLE, Proc. Roy. Soc. Med. **17**:74 (July) 1924.

A woman, aged 55, had follicular lesions of nine months' duration on the forearm, resembling lichen spinulosus, except that they were somewhat redder, with two accompanying patches composed of follicular lesions on the hairy scalp. On one of these there was no alopecia. On a portion of the second patch, in close juxtaposition with the follicular lesions, there was an area of cicatricial alopecia about the size of a quarter. The inference that the alopecia was really the result of follicular keratosis was rendered probable by the presence of the follicular lesions near it. The appearances presented by the

cicatricial alopecia were exactly like those of Quinquaud's disease, except that the latter often shows suppuration round the follicles, which was not the case here.

In discussion Dr. A. Eddowes said he thought the question whether the lesions were those of lichen planus or lichen spinulosus was largely one of anatomic distribution. On the hairy parts, there was a greater tendency for the lesion to be spinous, and on the sweat gland areas it was more likely to be planus. It was not uncommon to see scars on hairy shins from lichen like those in the scalp of this case.

PEMPHIGUS CONFINED TO THE MUCOSA. E. G. GRAHAM LITTLE, Proc. Roy. Soc. Med. **17**:75 (July) 1924.

This patient gave the history of having small blisters in the mouth nine years ago, and she had had no condition affecting the skin, only the mucosa. Five years before, she became blind, owing to contraction of the conjunctiva. She had similar inflamed atrophic patches in the mouth and also in the vulva, and the vaginal orifice was narrowed by the contraction to very small dimensions, so that it would barely admit the little finger. She was referred, as it was thought that it might be a skin condition. Ophthalmologists had made a diagnosis of essential shrinkage of the conjunctiva, which is a manifestation of pemphigus. In discussion, Dr. H. Semon said that a similar case was described in a recent number of the *Arch. für Dermatologie und Syphilis*, and it was there discussed in great detail. In that case, the lesion was proved to be pemphigus on account of the eruption subsequently appearing elsewhere on the body. The urine showed a marked diminution of sodium chlorid, and this was regarded by the author of the article as an essential point in the diagnosis. That deficiency might be investigated in the present case for a confirmation of the diagnosis. Dr. W. J. O'Donovan and Dr. Savatard had seen similar cases.

CASE OF UNUSUAL TOLERANCE TO CHRYSAROBIN. H. C. SEMON, Proc. Roy. Soc. Med. **17**:78 (July) 1924.

A patient with a more or less generalized psoriasis for nine years, while under the care of a physician in Jersey had been using increasing strength of chrysarobin ointments, until at the time of presentation he had been having daily inunctions of a 25 per cent. combination to the whole body, except the face and scalp. This was done in a nursing home under the author's control, and there had been little reaction, no sign of gastric or renal intolerance, and the psoriasis had involuted satisfactorily. Dr. Semon had been in touch with a firm of wholesale chemists who import the Goa powder from India. This substance, which is collected from the cavities in the trunk of *Andira araroda*, was originally imported from Brazil. The export duty payable in England resulted in the smuggling of the plant to England, where it is now a commercial asset, and where possibly deterioration due to altered climatic conditions or some other factor may be responsible for its apparently reduced efficacy. In discussion, Dr. Graham Little said he had found variation in the effect of chrysarobin, and it was largely a question of the quality of the drug, of which some inert samples had been put on the market in London recently.

GUY, Pittsburgh.

Two Cases of Cutaneous Sarcomatosis. J. Nicolas, J. Gaté, R. Gaillard and P. Ravault, Ann. de dermat. et syph. **5**:129 (March) 1924.

Two cases are reported in which the involvement was apparently primary in the subcutaneous tissue, and in which a fatal outcome ensued in a year and in three and one-half months, respectively. Histologically, the first case was of the fusiform and the second of the polymorphous type, a difference which, in the opinion of the authors, was probably due to the adaptation of the tumor cell to various environments.

Analogies in Blood Changes in Psoriasis and in Alopecia Areata in Nonsyphilitic Patients. A. Sicoli, Ann. de dermat. et syph. **5**:139 (March) 1924.

In a study of twenty-three cases of psoriasis and ten of alopecia areata, the author found from 6 to 9 and from 5 to 8 per cent. of eosinophils, and from 35 to 41 and from 28 to 37 per cent. of lymphocytes, respectively, except at the onset or during acute flare-ups, when both approached normal. This blood picture recalled that of chronic tuberculosis. Thus Sabouraud's impression of the existence of a relationship between alopecia areata and psoriasis is confirmed on hematologic grounds.

The Reaction of Sachs-Georgi. A. Starobinsky and L. Weyl, Ann. de dermat. et syph. **5**:150 (March) 1924.

The authors have found this reaction sufficiently specific, and generally less sensitive than the complement-fixation reactions, and advise its use in parallel with the Wassermann reaction as a check. They feel that the Sachs-Georgi reaction has yet to be fully evaluated, which can only be done in the light of more years of experience with it.

Traumatic Congenital Pemphigus with Lesions of the Parotids. A. Lyon, Ann. de dermat. et syph. **5**:163 (March) 1924.

A man, aged 45, had presented bullous outbreaks, with remissions, since the age of 2 years, the lesions usually appearing after local trauma. There was bilateral parotid enlargement. Both he and his mother presented dystrophy of all the nails, suggesting a familial defect, possibly of endocrinous origin. Nikolsky's sign was negative.

Late, Nonhereditary Traumatic Pemphigus. L. Chatellier, Ann. de dermat. et syph. **5**:168 (March) 1924.

In a man, aged 48, bullae had appeared on both hands for one year, and epidermal cysts had formed. The hands alone were affected. Nikolsky's sign was negative.

Cutaneous Myomas. L. Spillmann and P. Michon, Ann. de dermat. et syph. **5**:193 (April) 1924.

The authors report the case of a woman, aged 35, with a solitary myoma which had appeared in a vaccination scar two years after the virus had been introduced. During each pregnancy there were recurrent pains in the tumor, repeated five or six times every twenty-four hours, and lasting about twenty minutes each time. These paroxysms disappeared abruptly with the onset of labor, and did not reappear until the next pregnancy, except for the presence

of a local sensation of uneasiness noticed during the menstrual periods. The authors state that no recurrence followed the excision of the tumor. They review the literature on the subject of myomas, both single and multiple, and suggest that the former be called "solitary" or "sporadic" myomas and the latter "extensive myomatosis."

CONFIGURATE DERMATOSIS OF LICHENOID TYPE, WITH POSITIVE INOCULATION OF A GUINEA-PIG. FRANCO FLARER, Ann. de dermat. et syph. **5**:200 (April) 1924.

A youth, aged 18, said that during his childhood he had had cervical and inguinal lymphadenopathy with persistent sinuses. The sinuses finally healed, and one year later there appeared in the cervical region several rings of tiny follicular papules, most of which were crusted; at the time of examination the central areas were atrophic. The histologic picture was that of lichen scrofulosorum, although the location was atypical, and tubercle bacilli were recovered from an inoculated guinea-pig. The author feels that in this case the infection probably traversed the lymphatic vessels.

ORIENTAL BOIL: HISTOLOGIC STUDY AND LOCALIZATION OF THE PARASITES. PAUL VIGNE and E. PRINGAULT, Ann. de dermat. et syph. **5**:212 (April) 1924.

At the port of Marseilles, the authors have observed this condition in immigrants en route from Bagdad to America, and they report three of these cases, in which they have made fourteen biopsies. The histologic findings are described in detail. Plasma cells were found to be very scarce, and central necrosis appeared only in one specimen. The number of organisms was found to increase with the development of the lesion, and few or none were found at the periphery of the nodules.

CUTANEOUS ANOMALIES ASSOCIATED WITH PAROTID HYPERTROPHY. C. LAURENTIER, Ann. de dermat. et syph. **5**:240 (April) 1924.

In two cases of congenital hypertrophy of the parotid glands, pigmented nevi were found. In the first case, the nevi were small and few, and there was also leukoderma and alopecia areata; in the second case, there was a very large pigmented nevus of the thorax.

PREMYCOTIC ERYTHEMA. J. NICOLAS, J. GATÉ and P. RAVAUT, Ann. de dermat. et syph. **5**:257 (May) 1924.

The authors report a case of four years' duration, in a woman, aged 34, there being no tumor formation. Clinically, seborrheic dermatitis, leukemia cutis and lepra had to be considered in making a differential diagnosis. The histologic examination is reported in detail, the findings corresponding with those which, according to Darier's latest textbook, characterize the pretumor stage of mycosis fungoides, but which are not always present in these cases.

CONGENITAL FAMILIAL ATROPHY OF THE NAILS. J. A. PIRES DE LIMA, Ann. de dermat. et syph. **5**:266 (May) 1924.

A woman with normal nails gave birth to several sons whose nails were also normal, and to twin girls whose nails were atrophic. One of these daughters, in turn, gave birth to one son whose nails were normal and three daughters with onychatrophy.

PENETRATION OF PARASITES THROUGH THE SKIN. C. JOYEUX, Ann. de dermat. et syph. **5**:272 (May) 1924.

The author describes briefly the protozoa, helminthae, arthropoda and parasitic fungi which gain entry through the skin; the manner of infection is considered.

HYPERCHOLESTERINEMIA AND LIPOMATOSIS. R. BONNEFOUS and A. VALDIGUIÉ, Ann. de dermat. et syph. **5**:291 (May) 1924.

Five cases are reported, representing various types of lipomatosis, and the authors' findings lead them to conclude that in multiple familial lipomatosis there is a considerable degree of hypercholesterinemia, which is also found less markedly in other forms of lipomatosis.

PRURITUS. P. JOURDANET, Ann. de dermat. et syph. **5**:297 (May) 1924.

The author describes the pruritic reflex, a sympathetic activity comparable to the pilomotor reflex but differing in that it is homogeneous. That is, in the former, a sensation of pruritus somewhere excites a reflex sensation of pruritus, whereas, in the latter, a sensation of pruritus excites a motor response on the part of the arrectores pilorum.

UNEQUAL PARTICIPATION OF TWINS IN CONGENITAL SYPHILIS. OTTO HASLUND, Ann. de dermat. et syph. **5**:321 (June) 1924.

The boy was serologically positive, and presented a syphiloderm soon after birth and other stigmas later; the girl was always serologically negative, and showed no manifestation of syphilis, excepting a positive luetin reaction, which may have been nonspecific. Thus arises the question of germinative infection.

UNUSUAL FORMS OF LICHENIFICATION. ENZO BIZZOZERO, Ann. de dermat. et syph. **5**:331 (June) 1924.

The author describes a case of circumscribed hypertrophic lichenification of the scrotum and one of diffuse lichenification of the face, with a photograph of each. He feels that individual predisposition and regional predisposition are important factors.

LATE OSTEO-ARTICULAR CONGENITAL SYPHILIS RECOGNIZED AFTER SURGICAL INTERVENTION. ANDRE LERI and R. BARTHELEMY, Bull. Soc. franç. de dermat. et syph. **31**:112, 1924.

In a man, aged 25, the involvement was multiple and of seventeen years' duration, the right hand and forearm being especially affected. With sinus formation, tuberculosis was simulated, and surgeons were content with that diagnosis. Healing ensued under antisyphilitic treatment.

LUPUS VULGARIS TREATED WITH THE METHYLIC ANTIGEN OF A. BOQUET AND L. NEGRE. L. LORTAT-JACOB and L. BETHOUX, Bull. Soc. franç. de dermat. et syph. **31**:116, 1924.

In two severe cases, remarkable improvement followed the intramuscular administration of about 50 injections of the methylic extract of tubercle

bacilli, previously treated with acetone. The total amount of extract used was 25 c.c., and the injections were given twice a week in two courses, with the interval of a month intervening.

A Case of Parapsoriasis. Louste and Thibaut, Bull. Soc. franç. de dermat. et syph. **31**:119, 1924.

The author describes a generalized lichenoid eruption of ten years' duration, occurring in a man, aged 54. Histologically, there was some question as to the diagnosis.

Lichen Scrofulosorum Following Injection of Jousset's Vaccine. Milian and Perin, Bull. Soc. franç. de dermat. et syph. **31**:121, 1924.

In a child, aged 3, with tuberculous osteitis of the face, a typical outbreak of lichen scrofulosorum followed the day after injection of a vaccine composed of tubercle bacilli; histologic examination confirmed this diagnosis, giant cells being present. An exfoliative eruption supervened.

Icterus Due to a Hepatic Recurrence in a Case of Syphilis of Long Standing, Following Treatment with Mercurial Oil. Milian and Rivalier, Bull. Soc. franç. de dermat. et syph. **31**:124, 1924.

Three months after a series of mercurial injections had been given, jaundice appeared, and with it a positive Wassermann reaction in place of one which had hitherto been negative. With the second injection of neo-arsphenamin, the icterus disappeared.

Syphilitic Icterus Occurring as a Herxheimer Reaction During a Course of Treatment with Neo-Arsphenamin. Milian and Solente, Bull. Soc. franç. de dermat. et syph. **31**:126, 1924.

In a previously undiagnosed case of syphilis of six months' duration, jaundice appeared after the fourth injection of neo-arsphenamin. Under daily injections of mercuric cyanid, the icterus faded, and the arsenical treatment was resumed.

Toxic Icterus Due to Neo-Arsphenamin. Milian and Solente, Bull. Soc. franç. de dermat. et syph. **31**:128, 1924.

Jaundice appeared during the course of arsenical treatment, when the syphilitic lesions were disappearing; it was accompanied by a typical arsenical erythroderma and an eosinophilia.

A Cat with a Dermatosis Called "Dermite Lymphadenique." G. Thibierge and Leblois, Bull. Soc. franç. de dermat. et syph. **31**:130, 1924.

There was an eruption of large moist papules in the abdominal and crural regions, and the regional lymph nodes were enlarged. The appearance of the eruption simulated that of secondary syphilitic lesions. The etiology was obscure.

LINEAR ERYTHEMA. R. BARTHELEMY, Bull. Soc. franç. de dermat. et syph. **31**:131, 1924.

Around the shoulder there extended a threadlike pink to yellowish line, slightly elevated and perhaps papular in places, curving irregularly; it was about 30 cm. in length. On the chest was a similar line, which was not so long, and on the lower part of the back there appeared several sharply outlined, slightly scaly erythematous patches. The skin showed an urticarial tendency. No parasite was recovered from the lesions. The duration of the condition was eight days.

SYMMETRICAL CIRCUMSCRIBED KERATOSIS OF THE EXTREMITIES. LOUSTE and BIDERMANN, Bull. Soc. franç. de dermat. et syph. **31**:134, 1924.

In a patient who had syphilis and gonorrhea, for which he was treated with arsphenamin, the forearms, wrists and dorsa of the fingers and the knees, shins and sides of the feet were occupied by circumscribed keratoses, which had first appeared in 1917, two months after arsenical and mercurial antisyphilitic treatment had been administered. There was some uncertainty as to whether the lesions were arsenical, syphilitic or gonorrheal.

ARTICULAR MANIFESTATION OF LATE CONGENITAL SYPHILIS. LOUSTE and ROUGIER, Bull. Soc. franç. de dermat. et syph. **31**:137, 1924.

A man, aged 21, presented a bilateral hydro-arthrosis of the knees, of fourteen months' duration. Although the Wassermann reaction of the blood was negative, that of the joint fluid was positive.

ANORECTAL STRICTURE AND CHRONIC INFLAMMATORY LESIONS PROBABLY OF GONORRHEAL ORIGIN. LOUSTE and ANDRE BARANGER, Bull. Soc. franç. de dermat. et syph. **31**:140, 1924.

In a man, aged 41, there were perianal ulcerations and condylomatous vegetations; biopsy examination showed the presence of a chronic inflammatory process. The lesions being apparently not tuberculous or syphilitic, and antisyphilitic treatment having been of no avail, a previous dysentery or a gonorrheal infection were considered as possible etiologic factors.

TRICHOPHYTIC INFECTION OF THE EYEBROW AND PERIORBITAL REGION. LOUSTE and ANDRE BARANGER, Bull. Soc. franç. de dermat. et syph. **31**:143, 1924.

A circinate, papulosquamous and crusted pruritic patch of two and a half months' duration occurred in a young farmer. The causative organism was found to be a large spored trichophyton common to calves.

TREATMENT OF SMALL AREAS OF LUPUS VULGARIS BY WIDE EXCISION FOLLOWED BY SKIN GRAFTING. PAUL MOURE, Bull. Soc. franç. de dermat. et syph. **31**:145, 1924.

The wound is treated with zinc chlorid for fifteen or twenty days, together with heliotherapy, if possible, and antiseptic applications of surgical solution of chlorinated soda or iodoform are also used; then the graft is applied. In this way, the period of treatment is much shorter than that required for other curative procedures.

AZOOSPERMIA WITH NO DETECTABLE TESTICULAR LESION AND WITH CONSERVATION OF THE SECONDARY SEXUAL CHARACTERISTICS IN A MAN. CLEMENT SIMON, Bull. Soc. franç. de dermat. et syph. **31**:149, 1924.

The author presented his first case at Bordeaux in 1921. The second case occurred in a man, aged 46, whose father had apparently been infected with syphilis, since he had died of a ruptured aneurysm.

NITRITOID CRISIS FOLLOWING INJECTION OF BISMUTH. LEREDDE, Bull. Soc. franç. de dermat. et syph. **31**:152, 1924.

In a patient complaining of headache and vertigo, with syphilis of seventeen years' duration, a positive Wassermann reaction persisted after the administration of forty injections of neo-arsphenamin. Following the second intramuscular injection of a bismuth preparation, during which no blood had returned through the needle, an immediate reaction occurred, with engorgement of the skin, lips and tongue and brief loss of consciousness, followed by aphonia. The crisis lasted for two hours, and was followed by two days of lassitude. The author tends to attribute the accident not to bismuth, but to other substances used in the preparation, perhaps guaiacol or camphor.

MULTIPLE OSSEOUS SPOROTRICHOSIS WITH SPINA VENTOSA, SIMULATING TUBERCULOSIS. PAYENNEVILLE, Bull. Soc. franç. de dermat. et syph. **31**:153, 1924.

In a child, aged 3 years, the right foot and leg, both hands and the right forearm were involved, with sinus formation. The diagnosis was confirmed by cultures and by animal inoculation. Photographs and reproductions of the roentgenograms show the lesions.

SYPHILIMETRY IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS. GASTOU and BETHOUX, Bull. Soc. franç. de dermat. et syph. **31**:160, 1924.

The method of Vernes is considered to be useful only in cases of active syphilitic infection as a check on the severity of the infection and on the effectiveness of the treatment. It is not valuable in cases of syphilis of long standing latent or localized syphilitic infection, or congenital syphilis.

TABES WITHOUT CHANGES IN THE CEREBROSPINAL FLUID IN A NATIVE OF MOROCCO. LEPINAY and CASABLANCA, Bull. Soc. franç. de dermat. et syph. **31**:164, 1924.

The syphilitic infection was of twenty years' duration in this woman, aged 45, and the classical signs of tabes were present. The Wassermann reaction was negative. The patient's husband presented a tertiary cutaneous syphilid. Among native Moroccans, tabes is rare.

PARKHURST, Toledo, Ohio.

ACCIDENTS DUE TO LUMBAR PUNCTURE, AND THEIR PATHOGENESIS. P. PAGNIEY, Presse méd. **32**:151 (Feb. 16) 1924.

The accidents due to lumbar puncture are of various kinds. The most frequent are the mild symptoms — a transient headache lasting from several hours to a few days; vertigo, nausea, vomiting and slight elevation of temperature may accompany this headache. Less frequently lumbar punctures may be followed by more severe reactions. The authors encountered shock in an

arteriosclerotic patient, which was followed by a serious tachycardia which ceased shortly, but which was followed by excruciating pains in the lower extremities. In patients suffering with brain tumor, rapid or slow death has been observed exceptionally following lumbar puncture. There is a group of persons in whom lumbar puncture may be followed by serious consequences, as for example patients with septicemia. The author cites the experimental work of Wegeforth and Ayer, who showed that certain microbes may be introduced without harm into the veins of the cat, but when this injection was followed by a simple lumbar puncture, a fatal meningitis occurred. The tardiness of the appearance of the symptoms after lumbar puncture may be due to a flow of spinal fluid into the surrounding tissue after withdrawal of the needle. This after-flow of spinal fluid may create a marked hypotension of the cerebrospinal fluid. Hypotension causes noticeable hyperemia of the meninges. In order to avoid a flow of spinal fluid after withdrawal of the needle, the author recommends a very fine needle and that as few punctures as possible be made; not more than from 10 to 15 c.c. should be withdrawn. The patient should lie on the abdomen, with the foot of the bed elevated for several hours. Milian recommends that patients should assume a knee-chest position for one-half hour after lumbar puncture and then the ventral position for twenty-four hours.

Accidents in syphilitic patients in the secondary stage, in epileptic patients and in persons with hypotension of the cerebrospinal fluid are rather common. A second lumbar puncture and an injection of physiologic sodium chlorid solution should be made until the pressure of the spinal fluid is raised almost to normal. The intravenous injection of 500 c.c. of physiologic sodium chlorid solution according to the method of Weed and McKibben, or from 30 to 40 c.c. of distilled water, often relieves the tenacious headache. If these measures bring no amelioration, the cause of the disturbance is probably a secondary hypertension of the cerebrospinal fluid, and a hypertonic solution should be injected or ingested. The simplest procedure is to have the patient drink a small quantity of a concentrated (from 60 to 80 per cent.) sugar solution every fifteen minutes.

Syphilis and Angina Pectoris. L. Gallavardin, Presse méd. **32**:598 (July 16) 1924.

The syphilitic origin of aortic aneurysm and of a large majority of cases of aortic insufficiency is well established today. The question is still open as to whether syphilis is the cause of angina pectoris. As early as 1914, Gaucher and Cesbron found it to be a causal factor in eighty out of 100 cases. In examination of a series of 450 cases, the author arrived at the following conclusions:

First, angina pectoris associated with aortic lesions is extremely common. In the association of angina and aortic insufficiency, syphilis is almost the rule and the figures of 88 per cent. are reached. Syphilis is constantly found in all cases of angina associated with aneurysm of the aorta.

Second, in angina pectoris without an aortic lesion, the frequency of syphilis is much less, and the figures are 20 per cent. It should be noted that the earlier angina is developed, the larger is the proportion of cases due to syphilis.

McCafferty, New York.

CUTANEOUS LEISHMANIOSIS. G. MARIANI, Gior. ital. d. mal. ven. **65**:1581 (Oct.) 1924.

This is a report of a case of a chronic tumor formation in the lower lip which broke down, discharged and left an irregular ulceration. Leishman bodies were found in the secretion. The condition must be differentiated from syphilis and malignancy. Arsphenamin injections effected a complete cure.

TWO CASES OF FOX-FORDYCE DISEASE. E. FREUND, Gior. ital. d. mal. ven. **65**:1636 (Oct.) 1924.

The author reports in detail two cases of the rare papular lichenoid eruption of the axillae and pubes, first described by Drs. Fox and Fordyce. In his cases, there was a great deal of pigmentation and no pruritus. Histologically, the sections showed hyperkeratosis and slight parakeratosis, most marked at the follicular openings and sweat pores, acanthosis, cellular vacuolation which sometimes suggests vesiculation and changes in the corium, characterized by enormous dilatation of the sweat glands and periglandular infiltration of round cells. Mast cells were numerous and plasma cells scarce. The condition must be differentiated from lichen simplex chronicus and acanthosis nigricans. The author reviews twenty-seven cases reported up to the present.

SYPHILITIC ADDISON'S DISEASE. AUGUSTO ORO, Riforma med. **40**:890 (Sept.) 1924.

Oro reports three cases of typical Addison's disease due to syphilis of the suprarenal glands. Two of his patients were greatly improved by antisyphilitic treatment. The third was in such an asthenic condition and so far advanced that he died shortly after admittance into the hospital. Necropsy showed unmistakable findings of syphilis of the suprarenal glands.

MELANOPLAKIA OF THE MOUTH. G. ARMUZZI and R. STREMPEL, Riforma med. **40**:894 (Sept.) 1924.

This rare condition, of which the authors report three cases, consists of leukoplakic pigmented patches situated in the mucous membrane of the mouth. Histologically, the condition presents the same features of leukoplakia but there are numerous granules of pigment in the epithelial cells. Tobacco chewing seemed to be the etiologic factor in one case, while in another the patches began to appear after intensive bismuth treatment for syphilis.

PIEDRA IN ARGENTINA. C. ORIOL ARIAS, Prensa med., Argentina **11**:349 (Sept.) 1924.

The condition as observed in Argentina consists of small, oval, stone hard, grayish nodules varying in size from 0.5 to 2 mm. in diameter. These nodules surround the hair or appear attached to the side of it. As many as fifteen nodules may be found on one hair. The nodules are composed of masses of spores of polygonal outline and with a double membrane, measuring about 2 microns. Cultures in Sabouraud's agar are easily obtained. The author has not classified the fungus.

NITRITOID CRISIS. A. VERSARI, Tribuna med., Argentina **9**:1134 (Sept.) 1924.

This is a discussion of the different etiologic theories of the phenomenon known as nitritoid crisis, observed after the administration of arsphenamin injections. In the author's opinion, the crisis may be prevented by mixing the arsphenamin solution with the patient's blood in the injecting syringe and administering the injection slowly.

PARDO-CASTELLO, Havana.

BOWEN'S DISEASE. ERICH LANGER, Dermat. Wchnschr. **78**:417 (April 12) 1924.

The author reports the second case recorded as occurring in a native of Germany, the patient being a woman, aged 26, presenting a single lesion which was situated on the breast. This patch had first appeared during pregnancy, and an exacerbation had occurred during a subsequent pregnancy. Histologic study revealed the characteristic picture of Bowen's disease.

THE RELATIONSHIP OF SKIN DISEASES TO VITAMIN DEFICIENCY. ADOLF MESKA, Dermat. Wchnschr. **78**:552 (May 17) 1924.

Vitamin deficiency in a person apparently improves the soil for activities of animal or vegetable parasites, and therefore, especially in dealing with parasitic conditions, the diet should be investigated and changed if faulty.

HEREDITARY ANATOMIC ARRANGEMENT IN IDENTICAL TWINS FROM THE STANDPOINT OF AN INVESTIGATION OF THE PAPILLARY SYSTEM OF THE FINGERS. LEVEN, Dermat. Wchnschr. **78**:555 (May 17) 1924.

By a close study of the finger-prints of so-called "identical twins," the author has shown that there is always some difference in the arrangement of the papillary system in any two apparently similar persons. The findings in a series of cases are reported, and illustrative finger-prints are shown.

CHARACTERISTIC FUNGUS FORMS (BEFALLUNGSPILZE, SCHWÄRZEPILZE) ON THE SKIN OF COUNTRY PEOPLE. CLAMANN, Dermat. Wchnschr. **78**:584 (May 24) 1924.

Club-shaped forms and hyphae are described and illustrated. The organisms were found in erythematosquamous and pustular skin lesions, and also on the apparently normal skin and mucosae. Their pathogenicity is uncertain.

AN ENDEMIC OF MICROSPORON INFECTION OBSERVED IN LEIPZIG. H. SOLTMANN and O. DIETZE, Dermat. Wchnschr. **78**:601 (May 31) 1924.

Numerous cases have been encountered, especially in institutions, the causative organism being *Microsporon Audouini*, and the site of predilection the scalp. Secondary pyogenic infection occurred in some cases. No cases of trichophytid were seen. The mycologic features are described, and also the therapy. In four cases, the administration of epilating doses of roentgen rays was followed by signs of cerebral irritation, such as headache, apathy, a rise in temperature and vomiting, the last named symptom occurring about five or six hours after irradiation and persisting but a short time.

IMPETIGO HERPETIFORMIS-LIKE DERMATOSIS ACCOMPANYING A MEDIASTINAL TUMOR. A. BUSCHKE, Dermat. Wchnschr. **78**:633 (June 7) 1924.

An otherwise apparently healthy man, aged 52, had had signs of a mediastinal tumor, not aneurysmal, since May, 1923, and a vesicular and crusted eruption resembling that of impetigo herpetiformis since July of the same year. Under roentgen therapy the tumor disappeared, and the eruption faded, indicating the possibility of a relationship between the two conditions.

THE PARASITOLOGY OF "CREEPING DISEASE." M. O. LAPIN, Dermat. Wchnschr. **78**:573, 611 and 638 (May 24 and 31 and June 7) 1924.

According to the author, there are two forms of this condition: the superficial and the deep or hypodermal type. The superficial is the typical form, the egg being deposited by the fly usually on the surface of the skin, but possibly at times intracutaneously through a minute surface abrasion. The incubation period usually extends into the third week after inoculation, but when the skin is kept warm and moist this time may be shortened to six or seven days, and to four days if the inoculation has been intracutaneous. The lesions caused by *Gastrophilus hemorrhoidalis* occur principally on the face and buttocks, while *Gastrophilus equi* usually causes lesions on the extremities, and less frequently on the buttocks. According to the speed of extension, the parasite may be found from 0.5 to 1 cm. or more in advance of the progressing end of the line, during pauses it may be found at the end of the line. As a therapeutic measure, the intracutaneous injection of ether is recommended. Invasion of the hypodermal type may occur through the skin or by mouth.

EXPERIENCES CONCERNING THE PROSPECTS OF CURE IN THE TREATMENT OF EARLY SYPHILIS. A. BRUNS, Dermat. Wchnschr. **78**:661 (June 14) 1924.

During a period of five years, 295 cases of primary syphilis were treated, 100 of which are considered as satisfactory for evaluation. It is concluded that in early primary syphilis mercurial medication is not needed, arsphenamin, preferably silver arsphenamin, being the most effective therapeutic agent. In cases which have reached a somewhat later stage, the employment of mercurials becomes important.

INFLUENCE OF DIFFERENT TEMPERATURES ON THE OUTCOME OF THE WASSERMANN REACTION IN ACTIVE AND INACTIVATED SERUM. HERMANN FÖRTIG, Dermat. Wchnschr. **78**:668 (June 14) 1924.

In examining 819 serums, the author has concluded that the method of Jakobsthal, using a temperature of from 0 to 4 degrees C., and that of Graetz, with a variation of 0 to 37 degrees, with inactivated serum, give the highest percentage of positive results, especially the method of Graetz. It is suggested that the serologic variations may follow treatment. The author refers especially to "occult" variation in primary syphilis.

PURPURA ANNULARIS TELANGIECTODES OF MAJOCCHI. ROBERT BACK, Dermat. Wchnschr. **78**:693 (June 21) 1924.

A case is described, in a man, aged 45, the first manifestations having appeared as rust-colored macules on the lower extremities, and extended to the abdomen and the sacral region. Six weeks later, the gluteal region was

involved, with the characteristic ring-shaped petechiae. Histologic study showed the presence of changes in the endothelium of the blood vessels, with a perivascular infiltration.

A Case of Lichen Planus et Acuminatus on a Psoriatic Skin. F. Maerz, Dermat. Wchnschr. **78**:698 (June 21) 1924.

The condition appeared in a woman, aged 54, after the administration of solution of potassium arsenite (Fowler's solution). No histologic study was made.

The Benign Miliary Lupoid of Boeck. J. Arnsson, Dermat. Wchnschr. **78**:700 (June 21) 1924.

In a man, aged 37, the face, trunk and extremities were involved, the duration being one year. A histologic report is included.

What Are the Relationships Between Syphilis and Pernicious Anemia? Rahlwes, Dermat. Wchnschr. **78**:703 (June 21) 1924.

The author describes a case in which the two conditions were associated, and concludes that syphilis may have played an indirect part in the causation of the anemia.

Quantitative Diagnosis with Cerebrospinal Fluid. Hugo Hecht, Dermat. Wchnschr. **78**:723 (June 28) 1924.

The technic of the quantitative Wassermann test is described, and also that for the quantitative determination of the hemolysin.

Parkhurst, Toledo, Ohio.

Walter Frieboes' View of the Formation of Epidermis in the Light of Similar Histologic Consideration. W. J. Schmidt, Dermat. Ztschr. **36**:1 1922.

The author, on the basis of histologic study of the skin of reptiles, regards the epidermis as formed of cells alone. The connection between cells is a physiologic phenomenon. Tissue cultures are claimed to substantiate his view. In animals having but one layer of epidermis, there is no question but that the epidermis is made up of cells.

Reply to W. J. Schmidt's Paper. W. Frieboes, Dermat. Ztschr. **36**:81, 1922.

Frieboes reiterates his stand on the mesenchymal origin of the epidermis

Rebuttal to Frieboes. W. J. Schmidt, Dermat. Ztschr. **36**:88, 1922.

Schmidt maintains that there is no mesenchymal formation in the development of the cells of the epidermis.

Arsenic Carcinoma and Other Cutaneous Effects of Arsenic. Aage L. Fonss, Dermat. Ztschr. **37**:257, 1923.

A review is given of the literature on the effects of arsenic on the skin. The conditions reviewed include: arsenical poisoning in beer drinkers, arsenic pigmentation, pseudotabes arsenicosa, arsenical erythema simulating scarlatina

or even dermatitis exfoliativa rubra. Zosteriform eruptions due to arsenic and to arsphenamin are recalled, including cases which must be differentiated from variola, varicella and pemphigus or other bullous diseases. The problem of hyperkeratosis due to arsenic and its relation to precancerous dermatosis is discussed. Of twenty-four certain cases of arsenic carcinomas, fourteen were on the hands or feet. Multiple primary lesions were noted in fifteen out of twenty cases.

Bites of Scolopender and Scorpion Stings with Reference to War Experiences in Macedonia. Heinrich Meyer, Dermat. Ztschr. **38**:1, 1923.

Local symptoms of itching and swelling at the site, with redness and the single or double puncture were seen. The general symptoms were confused by the infectious diseases already present in the German prisoners of war. Wet dressings, especially weak alkalis, gave the best results. The literature is reviewed.

Dermatitis Dysmenorrhoica Symmetrica-a Disease sui Generis. R. Polland, Dermat. Ztschr. **38**:89, 1923.

The author states that since his earlier report on this condition, numerous other publications have placed the disease on an actual basis, and that there is no ground for believing that self-inflicted dermatosis or artificial dermatosis need be considered. A dysfunction of the ovaries is held responsible, and the result on the skin follows hematogenous carriage of the toxic substances from their source.

Psoriasis in an Infant With Well Marked Leucoderma Psoriaticum. Erich Hoffmann and R. Strempel, Dermat. Ztschr. **38**:193, 1923.

The authors report the unusual concurrence of two rare conditions in one infant.

Exfoliative Erythroderma in Childhood. R. Polland, Dermat. Ztschr. **38**: 201, 1923.

Report of a case of a child who, at 4 or 5 months of age, presented a typical erythema which was of three or four months' duration. There was no seborrhea close of the fifth and sixth summer of life, the child had a recurring general erythema which was of three or four months' duration. There were no seborrhea and no enlarged glands; the internal organs were normal and functioned properly during the interval of illness.

Investigation of the Serum of Pregnant Women with Chloasma Uterinum for Epinephrin. F. Fischl, Dermat. Ztschr. **38**:209, 1923.

Refractometric investigation after the method of Pulfrich on twenty-four pregnant women with chloasma uterinum, and twenty without the chloasma showed a distinct increase in epinephrin decomposition for the affected pregnant women. Only brunette nonpregnant, and never blond nonpregnant, women showed any decomposition. This investigation is thought to substantiate the contention of Biedls, Hofstatters, Königstein and others that there is some

connection between chloasma uterinum and the suprarenals. Whether the internal secretion of the suprarenals acts directly or reflexly through the sympathetic nervous system cannot be decided by the method of investigation pursued.

DOERR AND SCHNABEL EXPERIMENTAL EVIDENCE FOR THE HYPOTHESIS ON THE IDENTITY OF HERPETIC AND ENCEPHALITIS ENDEMICA VIRUS. ALFRED SCHNABEL, Wien. klin. Wchnschr. **36**:84, 1923.

The author bases his assumption on the histology of the pathologic lesions resulting from experimental inoculation of rabbits. Variations in incubation, clinical symptoms, cell character and localization were noted during the continued passage from animal to animal. The cell inclusions described by Lipschutz, Luger and Lauda were seen. A lethargic and a myoclonic type were distinguished clinically.

RECENT OPAQUE AND FLOCCULATION REACTIONS IN SYPHILIS. K. HAJOS and ST. HOFHAUSER, Wien. klin. Wchnschr. **36**:163, 1923.

The tests of Meinicke, Dold and Kahn were performed in 1,291 cases. The Wassermann reaction is more sensitive than the Meinicke or Dold reaction, which, on the other hand, appear more specific. The Dold reaction with formaldehyd control is more specific than the Meinicke. The latter gave a positive reaction in multiple sclerosis, pulmonary tuberculosis, arteriosclerosis, liver tumor and muscular rheumatism. The Dold reaction was negative in only one instance in which the Wassermann test was positive, a case of icterus catarrhalis. The flocculation reactions are not suitable for spinal fluid. Kahn's reaction is not specific. Flocculation reactions should be utilized only in association with the Wassermann reaction.

PRESENT STATUS OF INVESTIGATION OF EXPERIMENTAL HERPES AND ENCEPHALITIS. ERNST LAUDA, Wien. klin. Wchnschr. **36**:231, 1923.

The author is satisfied that the work has progressed sufficiently to establish the identity of the virus of herpes and encephalitis.

OSMOSIS FACTOR IN OSMOTIC THERAPY AND PROTEIN BODY THERAPY. CARL STEJSKAL, Wien. klin. Wchnschr. **36**:276, 1923.

The author's experiments with hypertonic salt solutions and their effect on the secretion of gastric juice through the nerve irritation leads him to believe that the use of protein bodies in therapy is likewise so regulated.

SYPHILIS AND PREGNANCY. H. THALER, Wien. klin. Wchnschr. **36**:287, 1923.

About 10 per cent. of pregnant women give a positive Wassermann reaction. Miscarriages in the later months of pregnancy are due to syphilis in 82 per cent. of the cases; and 80 per cent. of macerated fetuses may be traced back to syphilitic infection. Habitual early abortion is no indication of syphilis. For prophylaxis of fetal syphilis, the author recommends a five year interval between infection and marriage with intensive therapy and resultant negative Wassermann reaction. Even in negative Wassermann pregnant women, treatment during pregnancy is recommended.

GOODMAN, New York.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

ABUSE OF TUBERCULIN AS THERAPEUTIC AGENT. A. ARMSTRONG, Atlanta M. J. **28**:67 (Nov.) 1924.

Armstrong advises never to use tuberculin when there is an active tuberculous lesion in the lungs or other organs of the body. It is a dangerous remedy on account of its erratic action at times and the smallest possible dose should be used to avoid a general reaction.

PLEA FOR STANDARDIZED WASSERMANN TEST. E. H. RUEDIGER, Calif. & Western Med. **22**:548 (Nov.) 1924.

The old fashioned Wassermann test, the Herrold ring or contact precipitation test for syphilis and the Kolmer modification of the Wassermann test were compared by Ruediger with his method. He found great disagreement in the results obtained. His method was from fifty to one hundred times as sensitive as the old Wassermann test, from fifty to one hundred times as sensitive as the test proposed by Herrold, and from two to four times as sensitive as the Kolmer modification of the Wassermann test.

ERYSIPELATOUS NECROSIS OF EYELIDS. H. GIFFORD, Nebraska State M. J. **9**:447 (Nov.) 1924.

In Gifford's case the erysipelatous abscess formation and necrosis of the eyelids followed Vincent's angina. Recovery ensued.

ANTISTREPTOCOCCIC SERUM IN TREATMENT OF ERYSIPELAS. H. J. LAVENDER, Ohio State M. J. **20**:697 (Nov.) 1924.

Lavender has analyzed results in 250 cases of facial erysipelas, of which number 150 patients had the local applications and 100 had the combined local and serum treatment. The applications used aside from the soothing and greater comfort afforded the patient, prevent, or control to a great extent, the formation of abscesses. Only 7 per cent. of all the cases were victims of this sequel. In this series the Burrow's mercuric chlorid solution was selected only. During the period of desquamation, boric ointment, 5 per cent., was used. Lavender finds that there are decided advantages in the use of antistreptococcic serum in the treatment of facial erysipelas: The actual course of the disease and the period of convalescence are reduced. The treatment is well borne by the patient. The deleterious effects are almost nil. However, the serum is not effective as a preventive measure.

OCCUPATIONAL HAZARDS OF RADIOLOGIST. R. D. CARMAN and A. MILLER, Radiol. **3**:408 (Nov.) 1924.

Carman and Miller are convinced that many radiologists are being harmed in their daily work and are menaced by graver injuries. To avert these injuries it is necessary, first of all, that the radiologic worker be impressed so thoroughly with his danger that he will take adequate precautions. Either the methods of protection now in common use are not effective, or the worker is careless in their application. The worker should be shielded not only from direct rays, but also from secondary irradiation which may reach him from any angle.

GOODMAN, New York.

For the radiographer efficient protection can be secured by simple means, but in fluoroscopy and radiotherapy more elaborate measures are required. Protection from irradiation and prevention of electric shocks have been given more attention of late by the manufacturers of roentgen-ray apparatus. Even with all practicable safeguards, a certain degree of exposure cannot be evaded. Laboratories doing a large amount of work should, therefore, have a reserve personnel to permit alternation of service or frequent holidays. Workers should repeatedly be cautioned to receive the least possible amount of irradiation consistent with the performance of their duty. Modern life, regardless of occupation, has an abundance of risks, and additions are superfluous. Besides taking all reasonable precautions, workers should have frequent medical examination.

Sigma and Wassermann Reaction Compared in 1,000 Tests. J. W. Bigger, Irish J. M. Sc., p. 495 (Oct.) 1924.

The comparative results obtained with the Wassermann and the sigma reaction on 1,000 serums are recorded by Bigger. In this series, 14.6 per cent. of disagreements occurred. In sixteen instances some gross error had been made. In fifteen the Wassermann was incorrect; in one the sigma reaction. In an unselected series of cases for diagnosis, the disagreements were only 8.5 per cent. It is suggested that in primary syphilis the Wassermann reaction becomes positive earlier than the sigma reaction. The great majority of the disagreements occur toward the end of treatment, when the Wassermann reaction falls to a negative earlier than the sigma reaction. These results strongly suggest that the Wassermann reaction and the sigma reaction bodies are not identical.

Immunization by Way of the Skin. C. Gernez, Ann. de l'Inst. Pasteur. **38**:892 (Oct.) 1924.

Gernez injected human red corpuscles intracutaneously in rabbits, and obtained a production of hemolysins, which differed only quantitatively but not qualitatively from those induced by subcutaneous injection. A still weaker but distinct effect was produced by application of the corpuscles on the shaven skin as a dressing.

Mycetoma Involving Inguinal Glands. E. Burnet, et al., Arch. d. l'Inst. Pasteur de Tunis **13**:306 (Oct.) 1924.

This is the thirteenth case of Madura foot that has been under observation at Tunis. Glands in the thigh, inguinal and iliac regions have been invaded during the four years' course. Burnet, Broc, Brun and Jamin have been able to find only three similar instances on record of the spread of the fungus, but they think that the adenitis probably has often escaped detection.

Chancroid. C. Nicolli, et al., Arch. de l'Inst. Pasteur de Tunis **13**:1243 (Oct.) 1924.

Eight articles in this issue by Nicolle, Durand, Conseil, Jamin and others discuss the advantages of the Reenstierna intradermal differential test for soft chancre, and vaccine therapy. Instead of intramuscular or subcutaneous injection, they found the intravenous route for the streptobacillus vaccine preferable. They give the details of a number of cases which demonstrate the efficacy of this method, even for old and multiple chancroids with complications. They

describe the technic for isolating and keeping the Ducrey bacillus, and state that the vaccine from it is as active and as specific, while the technic of treatment with it is simpler in comparison to Reenstierna's antiserum.

INFLUENCE OF FATS ON TAR CANCER. J. LECLOUX, Compt. rend. Soc. de biol. **91**:1155 (Nov. 28) 1924.

Lecloux states that application of oleic acid delayed the development of experimental tar cancer in mice.

GENERAL PARALYSIS. S. R. MORENO, Medicina **5**:111 (Nov.) 1924.

Ramírez Moreno discusses prophylaxis in particular, saying that the fate of the syphilitic may depend on the treatment he gets in the first month after infection, and that general paralysis seems to be increasing in prevalence, invading even the aboriginal races. In Mexico, the records of the asylums show the increase. He urges diagnostic lumbar puncture in every one suspected of either syphilis or neuropathy, as the only means to ward off general paralysis later.

ANGIOKERATOMA. U. TOMASONE, Riforma med. **40**:1057 (Nov. 10) 1924.

Tomasone observed a case of this sequela of chilblains in a tuberculous man. The affection begins with red spots which proliferate and resemble warts, but become blanched after pressure. The disease has been described by Breda, and called angiokeratoma by Mibelli. It seems that a predisposition of the cutaneous blood vessels is necessary. Their dilatation is followed by a hyperkeratosis. Tuberculosis might play some part in it, although he found no histologic indications of it in the lesions. In spite of lack of direct evidence, he is inclined to regard them as tuberculids.

ELECTROCOAGULATION OF EPITHELIOMA IN TONGUE. CAPIZZANO, Rev. Asoc. méd. argent., Buenos Aires. **37**:33, 1924.

Capizzano applied electrocoagulation to an epithelioma of the tongue which was considered inoperable on account of the size, the enlarged glands in the vicinity, the age, and the poor general condition. He then excised the charred tissues, and the lesion rapidly healed while the glands returned to normal size. A small nodule six months later was treated in the same way, and the man has been clinically cured since 1918.

THE AORTA IN CHILDREN. E. A. and J. J. BERETERVIDE, Rev. Asoc. méd. argent., Buenos Aires. **37**:66, 1924.

The Beretervides now have a record of roentgenologic study of the aorta in 462 children with inherited syphilis. It has confirmed their previous announcement that the aorta is wider and casts a darker shadow than normal in children with inherited syphilis. The normal maximal diameter of the aorta in children is 1 cm. up to the age of 8, and 1.3 cm. from 8 to 14. When it is found wider than this, or abnormally opaque, they insist that treatment for syphilis is not only justified but imperative. This aorta roentgen sign of syphilis in children has never failed in all their experience. An exaggerated second sound at the left margin of the sternum and in the second or third interspace, with peculiar features, usually accompanied this aorta sign. Aortitis in adults frequently can be traced back to early childhood, when it might have been cured if it had been detected and perseveringly treated.

Recklinghausen's Disease in Children. Acuna and Bazan, Semana Med. **2**:813 (Oct. 9) 1924.

Acuna and Bazan describe eight cases of congenital Recklinghausen's disease, encountered recently. There was nothing to suggest a hereditary or familial character. In two of the children, there was malformation of the spine or chest, in addition to the manifestations of the disease; in three, there was evidence of endocrine derangement; and in two, one in each of these two groups, congenital syphilis was plainly manifest. In children, Recklinghausen's disease is usually of an incomplete abortive type; only the characteristic spots on the skin were varied, explaining why nonsymptomatic Recklinghausen's disease in children is so often overlooked.

Treatment of Syphilitic Aortitis. G. Wodtke, Deutsch. Arch. f. klin. Med. **144**:357 (July) 1924.

Wodtke advocates combined neo-arsphenamin treatment for syphilitic aortitis. The treatment should be undertaken as early as possible. The possibility of syphilis should be taken into consideration whenever any of the symptoms of aortitis are found. Syphilitic patients should always be reexamined for aortitis.

The p_H of Skin Surface. A. Memmesheimer, Klin. Wchnschr. **3**:2102 (Nov. 11) 1924.

Memmesheimer estimated the hydrogen ion concentration of the surface of the skin by dropping indicators on it. The normal p_H figures are between 5.2 and 5.8. Roentgen irradiation was followed by an alkaline shifting which was most marked after twenty-four hours. Universal eczema, psoriasis and toxic exanthem gave normal figures.

Tabes and Mesaotitis. S. Kessler, Klin. Wchnschr. **3**:2146 (Nov. 18) 1924.

Kessler found thirty-nine cases of syphilitic mesaotitis among fifty-nine necropsies of tabes. The affection of the aorta is usually milder than in other syphilitics because the patients cannot lead a strenuous life, are treated for syphilis, and because the visceral sensibility is impaired.

Roentgen Surface Treatment. E. Kuznitzky, Klin. Wchnschr. **3**:2148 (Nov.) 1924.

Kuznitzky uses exclusively filtered roentgen rays (0.5 mm. aluminum) for treatment of dermatoses. This method prevents the erythema, with subsequent remote atrophy of the skin and teleangiectasia which is frequent with the unfiltered rays. Leschinski's auto-experiments confirmed this view.

Congenital Syphilis. S. Buttenwieser and H. Biberfeld, Med. Klin. **20**: 1649 (Nov. 23) 1924.

Buttenwieser and Biberfeld observed fever of long duration in two boys, aged 10 and 11, with enlarged liver and congenital syphilis. The diagnosis of tuberculosis had been made in both patients, although one had no tuberculosis at all, and the other only as a complication. The fever in these cases is high, daily intermittent, and lasts for days or weeks. Chills and night sweats may occur. Specific treatment of the syphilis is of great value.

POSTOPERATIVE IRRADIATION. L. SIMON and W. WOLLNER, München. med. Wchnschr. **71**:1639 (Nov. 21) 1924.

Simon and Wollner recommend irradiation with small doses (far below the cancer dose) after radical operations on cancer of the breast. The treatment should be given at first every six weeks, later at longer intervals for a year or year and a half.

HISTOLOGIC STUDY OF CAUSE OF CANCER. GRÜTZ, Ztschr. f. Krebsforsch. **21**: 415 (Oct. 22) 1924.

Grütz' microscopic research in three cases of Bowen's precancerous dermatosis has convinced him that Bierich's theory of a pathologic transformation of the "protoplasm system" in malignant disease deserves greater attention. It calls for research on cancer and precancerous conditions from a new standpoint.

MORPHOGENESIS AND HISTOGENESIS OF EXPERIMENTAL CANCER. W. STEFKO, Ztschr. f. Krebsforsch. **21**:432 (Oct. 22) 1924.

Stefko found it impossible to induce tar cancer in the skin of amphibians (frogs and toads). A toxic action on the tissues below and on the heart, liver and lungs was apparent, and lymphangiomas sometimes developed. The animals all died. He adds that lymphangiomas from tar have not been encountered in tar cancer in mammals.

MALARIA TREATMENT OF PARALYSIS. H. BONDY, Casop. lek cesk. **63**:1699 (Nov. 22) 1924.

Bondy has five years of experience of treatment of progressive paralysis with malaria inoculations. He observed in a few cases improvement of the pupil reaction and of the knee-jerk. The handwriting and speech were more constantly improved.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Monthly Meeting, Oct. 7, 1924

PAUL E. BECHET, M.D., *Chairman*

NASAL CHANCRE WITH SEVERE MANIFESTATIONS AND AN ODD HISTORY. Presented by DR. PAROUNAGIAN.

Mrs. H. R., aged 28, was referred to the Bellevue Syphilis Clinic on October 1, 1924, with a four plus Wassermann reaction. She gave the following history: The patient was a practical nurse, and was attending a colored woman during her confinement early in June, 1924. During the delivery, the membranes ruptured, and the fluid splashed over her face. The colored woman was said to have a four plus Wassermann reaction, and she had a macerated baby. In the early part of July, 1924, the patient developed a sore nose, for which condition she went to a nose clinic. During her attendance at the clinic the lymphatic glands at the angles of the jaw became greatly swollen. A Wassermann test was reported negative, and she was referred to the surgical ward, where a portion of the swollen glands were removed (left side). The condition did not improve; the woman felt worse day by day. Finally another Wassermann examination, on Sept. 11, 1924, revealed a four plus reaction, for which she was referred for treatment. On admission, she had a papular, non-itching rash on the forehead, tip of the nose and nasolabial folds, and a papular eruption, mostly on the back. The glands at both angles of the jaw were markedly swollen, more marked on the left than on the right. Both tonsils were greatly enlarged and ulcerated; there were mucous patches on the tongue. The infiltrated remains of a sore was detected at the left nostril on the septum, which was believed to be the remains of a chancre. The genitals were entirely free from lesions. The possibility of tonsillar infection was considered, as both tonsils were ulcerated, but the patient insisted that her nose became sore first, leading to the belief that the infection took place in the nose first.

ARGYRIA. Presented by DR. CHARGIN.

O. S., a man, aged 39, married, a leather bag maker, about eight years ago began the use of a spray solution for repeated attacks of hoarseness. He made use of the spray for a period of a month each year for several years. He had not used the spray solution for about three years. He noticed a change in the color of his skin about three and half years before presentation. At the time of presentation he showed a generalized argyria, most marked on the face and hard palate, although the rest of the body was affected to a less extent. The analysis of the solution that he employed as the spray showed it to contain 5 per cent. argyrol.

DISCUSSION

DR. WOLF asked whether Dr. Chargin was certain about the use of argyrol in this particular case. Perhaps it was a silver nitrate solution that was used.

Dr. Pollitzer said that numerous cases of argyria had been reported following the use of argyrol, especially in ophthalmologic practice.

Dr. Chargin replied that there were many cases of localized argyria reported in the literature, from local use in the eye, nose, or mouth; but that cases of generalized argyria resulting from the use of argyrol were rare. In looking through the literature, he had been able to find only three cases on record. The solution used by this patient was analyzed and found to contain 5 per cent. argyrol.

Neurodermite (Circumscribed) or Nevus Verrucosus. Presented by Dr. Wise.

A young man, aged 19, native born, a collector, for the past ten years had noticed a patch about 2 by 1 inches (5.08 by 2.54 cm.) in diameter, which was occasionally itchy. It was located below the left patellar region, sharply marginated, and consisted of conical, lichenified and scaly lesions. A report on the biopsy taken had not been received as yet.

DISCUSSION

Dr. Pollitzer said that clinically he would not hesitate to make a diagnosis of nevus. To his mind, neurodermite was ruled out by the absence of any papules of lichen simplex, which might always be seen at the periphery of the patches. He thought the entire lesion ought to be excised, because in that location a hard horny layer might easily be irritated and cause atypical proliferation of the underlying epithelial structures

Acute Pemphigus. Presented by Dr. Wolf.

H. M., a man, aged 54, a widower, born in the United States, had been healthy all his life. His present trouble dated back five weeks. The eruption first appeared on the back of the neck, and in three days it covered almost the entire scalp and face. During the past three weeks, the neck, upper part of the chest, both scapular regions and buttocks had become affected. The eruption was essentially a bullous one, the lesions varying in size from that of a split pea to that of a coffee bean. The blebs came out in crops or singly, and varied as to springing from apparently normal skin or from an erythematous base. There was no pruritus, and Nikolski's sign was absent. The Wassermann test was negative.

DISCUSSION

Dr. Lane said he thought that there must have been a mistake in the recording of the diagnosis, as the case had none of the characteristics of acute septic pemphigus. A patient with that condition would not be wandering around with no rise in temperature. He had thought it might be a case of Duhring's disease; if not, a case of chronic pemphigus.

Dr. Wise agreed with Dr. Lane that it might be a case of Duhring's disease. The only thing against that was the absence of itching, but that symptom was sometimes absent in Duhring's disease. Distribution of the lesions was also in favor of Duhring's disease.

Dr. Pollitzer said he thought the condition was pemphigus — acute only in the sense that it was a recent, beginning pemphigus. He did not see on what a diagnosis of dermatitis herpetiformis could be based. The man had a lot of blisters around the neck, on the scalp, chest, etc. For the diagnosis of

Duhring's disease there was nothing but the crop of bullae; no pain nor itching; no herpetic grouping etc.

Dr. Levin agreed with the diagnosis as presented. There were no polymorphous lesions, nor itching, nor pain, nor grouping of Duhring's disease. Nikolski's sign was present. As for eosinophilia, pemphigus and dermatitis herpetiformis both showed increased eosinophilia.

Dr. Scheer said the patient showed only one feature of Duhring's disease —blisters, and as a rule the disease showed multiform lesions; but the moderately advanced age of the patient, the absence of itching, and the distribution of the blisters were all in favor of pemphigus, as well as the presence of Nikolski's sign.

Dr. Bechet said that the early stages of these bullous eruptions were frequently confusing, and it was of interest to note the different impressions given by different observers. He had seen the patient twice at the University and Bellevue Clinic, in a very good light, and had tested carefully for Nikolski's sign but had found it negative. The lesions were surrounded by an erythematous areola, and he had noted some papules on the neck and sides of the face. At that time, he did not note any bullae arising from apparently healthy skin; in his opinion, an exaggerated importance was ascribed to this symptom in the diagnosis of pemphigus. He was much more inclined to the diagnosis of erythema multiforme bullosum than pemphigus. In his opinion, in view of the objective symptoms, the diagnosis of dermatitis herpetiformis was not tenable.

Dr. Highman said that he thought the condition was pemphigus.

Dr. Wolf said that he would like to explain the title of acute pemphigus; by that he did not mean to use the term acute in the sense of the severity of the condition, but rather in the sense of time, the patient having had the condition for only five weeks; therefore it would be better to call it an early pemphigus. The diagnosis of dermatitis herpetiformis could not be entertained for the reasons given by Dr. Pollitzer. The primary lesion was a bulla, and there were no lesions with erythematous bases. He had not been able to detect Nikolski's sign, nor had there been any itching at any time. The Wassermann test was negative. The most interesting point was that the man had been healthy and well until about five weeks ago, when he woke up one morning with these blisters on the neck, which spread rapidly. As yet there were no mucous lesions, but he was getting new lesions all the time on different areas, and the old ones were involuting.

Recurrent Roseola and Other Secondary Manifestations of Syphilis. Presented by Dr. Parounagian.

W. K., a man, aged 34, born in the United States, married, first seen at the Bellevue Syphilis Clinic on Jan. 14, 1924, then had a phimosis of two and one half months' duration; the incubation period was not noted. He also had general adenopathy and roseola; the Wassermann reaction on Jan. 14, 1924, was four plus. He was immediately placed under treatment, which consisted of eight arsphenamin and nine mercuric salicylate injections. He made his last visit on Aug. 8, 1924. The patient discontinued his visits of his own accord. He returned on the day of presentation, Oct. 7, 1924, with recurrent roseola, moist papules about the genito-anal regions and laryngitis. He gave the duration of these recurrences as about two weeks.

DISCUSSION

DR. CHARGIN inquired as to the type of recurrent roseola.

DR. POLLITZER said that every one knew what was meant by the term recurrent roseola. He understood that this man came under observation in January, 1924, was treated with injections of arsphenamin and mercury, and had just developed roseola, etc. A recurrent roseola usually made its appearance much later after treatment, sometimes after an interval of several years. Dr. Pollitzer then asked Dr. Parounagian for information about the treatment, and said he was very much inclined to the opinion that the condition presented was the result of inadequate treatment.

DR. SCHEER said that recurrent roseolas were not rare now; before the arsphenamin era, under treatment with mercury injections, they were unusual. These cases had been described as late as eight years after the initial lesions. In the recurrent roseolas, the lesions were larger than in the secondary outbreak. One patient, referred to Sabouraud, received very thorough treatment for three years, and then returned to New York and had three or four recurrences. The usual recurrence of secondary lesions took on a papular form, the papules being arranged in circles. Dr. Scheer said that he did not think the appearance had anything to do with adequacy or inadequacy of treatment.

DR. CHARGIN said that he had not read the history, and desired to know whether this was an early secondary recurrence or a recurrence of a macular eruption such as was seen in late syphilis — so-called tertiary roseola.

DR. HIGHMAN said that he did not know how it was possible to differ so greatly on a question of fact as he differed with Dr. Chargin. It was the first time in his life he had ever heard a recurrent roseola described as tertiary. He had a case which almost duplicated the one mentioned by Dr. Scheer in frequency of recurrences. The patient was under observation for three or four years and received energetic treatment, and had at least three separate recurrences. He believed that the recurrent roseolas represented a peculiar reaction of the patient to the spirochete. Instead of the usual cutaneous responses, he simply relapsed to the simple type of the macule. Perhaps if the man had not received sufficiently energetic treatment, he would have had a severer reaction.

DR. PAROUNAGIAN, answering Dr. Chargin as to what he meant by recurrent roseola, said that this patient had a chancre, roseola, mucous patches, general adenopathy and a four plus Wassermann reaction in January, 1924. He received eight arsphenamin and nine mercuric salicylate injections, and then discontinued treatment of his own accord and was not again seen until he had these recurrent symptoms. Most of the recurrent roseolas observed by Dr. Parounagian had been cases in which chancre had been followed by roseola, and after six months or a year a macular eruption appeared without a second chancre. The difference in the recurrent roseola was its brighter red color and circinate character. His personal observation was that most of the recurrent roseolas occurred within one year after infection, with one exception, in which the duration was four years and seven months. Replying to Dr. Pollitzer's question regarding the size of the dose of arsphenamin, Dr. Parounagian said that in a clinic like that at Bellevue in which 150 or more injections were given in a day, and with all kinds and conditions of patients, many of whom returned to their occupations after receiving treatment, it would be rather unsafe to give massive doses; the average dose of arsphenamin was 0.3 gm.; neo-arsphenamin, 0.45 gm.; and silver arsphenamin, 0.2 gm.

If that precaution were not observed, there would probably be many accidents. Replying to Dr. Pollitzer's query as to whether a Wassermann test was made at the end of the course of treatment, Dr. Parounagian said that the patient had discontinued treatments before the course was completed.

CHRONIC EDEMA OF THE EYELIDS. Presented by DR. WISE.

M. R., a man, aged 50, Canadian, a saw-filer, presented a plain edema of the eyelids with slight redness. The condition had existed for one year. The man gave a history of erysipeloid attacks, but no involvement of any of the sinuses had been detected.

SCLERODERMA AND SCLERODACTYLIA. Presented by DR. WISE.

P. B., a negro woman, aged 35, born in the United States, complained of her condition for seven years. Her mouth had a pinched appearance. There was depigmentation in patches and pin-point areas on the chest and neck. There were also depigmented lines on the back of the trunk. Beginning on the forearms and extending to the wrists, there was a depigmented stippling with a hidebound condition of the entire skin, making her unable to clench her fists. The tips of her fingers were clubbed, and she complained of loss of sensation. There were no signs of leprosy. She failed to have her blood taken for a Wassermann test.

CUTIS GYRATA, LEUKODERMA, AND PRURITUS OF THE GENITALS. Presented by DR. ABRAMOWITZ.

W. P., a man, aged 36, a Spaniard, restaurant worker, presented on the back of the scalp transverse folds of skin extending from ear to ear. He had noted this as far as he could remember. In addition he had depigmented patches on the buttocks, abdomen and chest, rather symmetrical, but most marked on the right side of the body. The pruritus which was around the genitals was of two months' duration and revealed no lesions. The Wassermann test was negative.

PHENOLPHTHALEIN ERUPTION. Presented by DR. FELDMAN.

J. G., a man, aged 34, came to the Beth David Dispensary the early part of August, 1924, complaining of severe itching and also of some pain of the joints. There was an eruption on the body and on the extremities. It consisted of very large reddish-blue patches, some of which were slightly raised above the level of the skin. After about one week, the itching subsided, and there was marked scaling of the patches; but no evidence of scaling was present on the intervening normal skin. The color changed to a bluish gray. This condition continued until early in September, when, as the patient stated, after taking a dose of Marmolax the itching began again. On examination, the same condition was found as on the previous occasion. Most of the old patches became reddened, and several new ones appeared. This again went through the same stages as the previous attack. As presented, the patches were much lighter in color than they had ever been before.

CONGENITAL SYPHILIS WITH ACTIVE LESIONS ABOUT THE MOUTH. Presented by DR. PAROUNAGIAN.

R. M., a girl, aged 5 years, seen at the Bellevue Clinic on Aug. 27, 1924, presented active condylomatous lesions about the mouth, which were of about

three months' duration. The Wassermann examination made on admission was reported four plus. The records showed that her sister, who was 9 years old, was referred about two years previously from the Bellevue Eye Department for treatment. This child then had interstitiitial keratitis with a four plus Wassermann reaction. The father and mother also gave four plus reactions, and were also placed under treatment.

Double Vulvar Chancre; Condylomas and Gonorrhea in a Colored Child 6 Years of Age. Presented by Dr. Parounagian.

D. M., a colored girl, aged 6 years, born in the United States, was referred to Bellevue Syphilis Clinic for an opinion on Sept. 25, 1924. Examination revealed two typical chancres, the larger sore on the right labia majora and the smaller one on the left labia majora. There were extensive condylomas about the genito-anal regions and profuse discharge which was proved by microscope to be gonorrheal. Dark-field examination was positive for *Spirocheta pallida* and the Wassermann test was reported four plus. The child gave a history of attempted rape.

Universal Alopecia. Presented by Dr. Parounagian.

R. T., a girl, aged 13 years, Italian-American, was referred by her physician. The condition had existed for the past seven years in spite of treatment by a number of private physicians. When first seen on May 27, 1924, she had practically no hair on the scalp, left axilla and half of the pubic region (left side). Since then, while under treatment, she began to lose the left eyebrow also. The mother said that the patient had had a fall and shortly after that an attack of diphtheria; thereupon the hair came out in large quantities. The girl appeared to be in good health, except that she was nervous, and her sleep was restless. Her treatment consisted of Alpine sun lamp, and applications of b-naphthol and sulphur ointment; internally, thyroid in small doses and tonics were given. Although she had recovered some of the hair on the scalp, the improvement was not extensive.

Chancre of Lower Lip. Presented by Dr. Parounagian.

C. De G., a man, aged 21, born in the United States, single, a barber, was seen at Bellevue clinic on the day of presentation (Oct. 7, 1924). He exhibited a well defined circular sore on the median line of the lower lip. The duration was stated to be three or four weeks, and the source of infection could not be ascertained. Dark-field examination was positive for *Spirocheta pallida*. No secondary manifestations could be detected. The interesting feature of this case was that the patient came to us without the active secondary infections as most patients with chancres of the lip do. The results of the Wassermann test had not yet been reported.

Atrophia Cutis Maculosa. Presented by Dr. Parounagian.

A. L., a man, aged 27, a Porto Rican, single, was first seen at Bellevue clinic on June 28, 1923. Venereal history was denied. Examination revealed innumerable whitish scarlike lesions located on the chest and back; some were raised, others slightly depressed. He experienced no discomfort, and believed the duration was about two years. In spite of his denial of venereal history, a well marked scar was detected on the prepuce near the frenum, and the

Wassermann test on the day of admission was reported four plus. He had received two courses of arsphenamin and mercury injections, with no apparent change in the skin lesions.

MEATAL CHANCRE WITH SECONDARY INFECTION. Presented by DR. PAROUNAGIAN.

K. M., a man, aged 29, a Swede, a sailor, was admitted to the hospital on Oct. 6, 1924, with the following history: Six weeks after exposure, he noticed a sore at the meatus. The sore was of two months' duration. Dark-field examination for *Spirocheta pallida* was positive on admission. He also presented a generalized macular eruption including the palms and soles. Results of the Wassermann test had not yet been reported.

PAPULOSQUAMOUS SYPHILID OF GLANS PENIS (TERTIARY SYPHILIS). Presented by DR. PAROUNAGIAN.

J. W., a man, aged 64, German, single, was admitted to the Bellevue Clinic, Sept. 22, 1924. He gave a history of chancre on the prepuce twenty-five years previously, and had been treated for a short time. The lesion were confined to the glans penis, and the duration was about two months. The Wassermann test was reported four plus. The patient had not been exposed for three years.

SECONDARY SYPHILIS WITH PUSTULAR SYPHILODERM OF THE PALMS AND SOLES AND MULTIFORM ERUPTION OF THE BODY. Presented by DR. PAROUNAGIAN.

G. H., a man, aged 54, born in the United States, admitted to the Bellevue Clinic on July 29, 1924, gave a history of exposure two months previously, and a genital sore of three weeks' duration. Examination revealed a large chancre of the sulcus which had become gangrenous, and the organ was edematous. He had been treated by a private physician and three dark-field examinations at the clinic were negative. The Wassermann examination on July 29, 1924, was negative. A second Wassermann test six days later was one plus, and as the process was advancing too rapidly, it was decided to give him a dose of neo-arsphenamin, which benefited him markedly. Unfortunately, the patient remained away for more than six weeks. On his return on Sept. 25, 1924, his Wassermann reaction had become four plus, and he presented a profuse eruption consisting of lenticular, papular, pustular and squamous lesions, with most unusual palmar and plantar syphilids.

REPORT OF CASES PREVIOUSLY PRESENTED.

DR. PAROUNAGIAN reported on two cases of pellagra which he had presented at the May meeting of the Section, at which the diagnosis was doubted by some. The majority diagnosed them as "erythema multiforme bullosum," as there were bullous lesions on the dorsum of both hands. The diarrhea of which the patients complained was charged to their having taken cathartics. The female patient died twenty-four days after presentation, and necropsy, which was made by Dr. Douglas Symmers, Director of Laboratories at Bellevue Hospital, was as follows:

"Alice A., aged 42, died May 27, 1924. The body was that of a woman 42 years of age, 163 cm. in length. The skin covering the back of both hands up to the point about 3 cm. above the wrist was denuded, leaving a vivid red surface. In the crease of the thigh on both sides, that is to say, between the thigh and labia majora, were linear, streak-like, bright red areas of excoria-

tion which extended downward and were lost in the general direction of the perineum. The tongue was slightly reddened and roughened. On opening the body, no noteworthy naked eye changes were detected other than pseudomembraneous gastritis and colitis. Microscopic examination of the skin showed rarefaction of the surface epithelium, beneath which the subcutaneous connective tissues were moderately rich in cells of the fibroblastic type. In the connective tissues were numerous dilated and distended venules, thus accounting for the reddish lesions. Practically identical microscopic changes were found in the mucous membrane of the tongue. Microscopic examination of the gastrointestinal mucous membrane showed superficial areas of necrosis with marked injection of the smaller blood vessels in the mucous membrane and numbers of dilated mucous tubules. The latter are quite characteristic and constant in pellagra and do not occur in any other condition with which I am acquainted. These small cystlike dilatations of the mucous tubules frequently contained quantities of thin mucinous material imbedded in which were greater or less numbers of well preserved polymorphonuclear neutrophiles."

The male patient improved sufficiently to leave the hospital.

Dr. Parounagian further stated that since spring he had seen about a dozen cases at Bellevue Hospital, and had personal knowledge of about six deaths from pellagra. At least three of these patients had never been South. He was of the opinion that these cases often were not recognized.

The following cases were also presented from the Vanderbilt Clinic by Dr. Wise: Recklinghausen's disease; mycosis fungoides; granuloma annulare; leprosy; lupus erythematosus; acrodermatitis chronica atrophicans.

Oscar L. Levin, M.D., Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 15, 1924.

James Herbert Mitchell, M.D., *Presiding*

A Case for Diagnosis. Presented by Dr. Senear.

A railroad man, aged 26 years, had had a small nodule in front of the left ear at birth. This broke down a year later and "discharged water." By the time he was 6 years old, this lesion had reached the size of a silver quarter, and was then removed surgically. It had not recurred, although the patient was at times able to express a cheesy substance with a foul odor. About one year before presentation, he developed an enlargement just in front of the right ear, which broke down and discharged purulent material. This lesion had been removed three times but still discharged a thin material.

DISCUSSION

Dr. Wile said that from the description of the case and character of the lesions he believed it was a localized tuberculous sinus.

Dr. Foerster said he thought that from the history, the persistence of a discharge which varied in character, and above all from the site occupied by the lesion, it was justfiable to regard the condition as a congenital defect, and that it was a branchial fistula. Such fistulas are found most often opening at one of three levels on the side of the neck, and less often at the ear.

Dr. Senear thanked Dr. Foerster for his suggestion, and said that at the Illinois Central Hospital the lesion had been regarded as a sebaceous cyst, which diagnosis seemed untenable, but he had not thought of a pre-auricular remnant.

Acrodynia (?). Presented by Dr. Olmsted (For Drs. Oliver and Finnerud).

An Italian boy, aged 5 years, had a disorder that was said to have been present at about the sixth month of life. Other children in the family were living and well, and the family history was negative.

The disorder began with marked scaling of the scalp, which later affected the palms, soles, chin and anus, the scalp lesions gradually clearing. The areas affected had never been entirely clear, although they had improved at times. When the child was examined three weeks before presentation, there were hyperkeratotic fissures of the palms and soles and some bloody crusting. The sides of the fingers and hands, as well as those of the feet and soles, were similarly involved; but the dorsal surfaces were spared. The margins of the lesions were made up of patulous follicles. The skin about the anus for several centimeters was grayish-white to red, and eroded. There was a band which extended across the chin from one side of the mouth to the other, which was thickened, somewhat hyperkeratotic and crusted. At the time of presentation, there was slight scaling in the scalp, which was not noticed at the former examination. The skin was generally dry, and there were several areas on the trunk and extremities in which the mouths of the hair follicles were hyperkeratotic. The child had developed slowly and had a sluggish pulse. His appetite was fair. Urinalysis was negative; there was a leukocytosis of 20,000; the differential count, the red blood and hemoglobin were practically normal. There was no change in the blood chemistry. The Wassermann reaction on the blood and spinal fluid was negative, as were the Pirquet and other tests for tuberculosis.

DISCUSSION

Dr. O'Leary said he thought that the patient's case resembled the case of cutaneous thrush reported in the *Archives of Pediatrics* last spring. Even though the scrapings from the hand were reported as negative, he felt that in view of the clubbing of the fingers the sputum should also be examined for mycelium.

Dr. Harry R. Foerster said he thought that the condition greatly resembled an erythredema, or so-called acrodynia. The only point opposed to this diagnosis was the chronicity of the cutaneous lesions. Acrodynia is considered to be a self-limited disease which terminates within a few months to a year, but in this case the lesions had been present for four or five years. All the other characteristic symptoms shown by this child, such as its peculiar mental and physical attitude, the necessity of forced feedings, the complaint on being handled and the type of skin lesions were typical of erythredema. As this condition is thought to be due to a toxic degeneration in the peripheral nervous system, Dr. Foerster saw no reason why it could not be of greater chronicity than past reports indicated.

Dr. Wile asked Dr. Foerster whether in any of the cases he had studied there had been lesions around the rectum. He was impressed with the fungating lesions around the rectum in the present case.

Dr. Harry R. Foerster replied that in one case observed by him there were lesions around the buttocks and prolapse of the rectum. He had been told that this was a not uncommon symptom. He thought perhaps this child

had had a prolapse, and on account of straining at stool a dermatitis had developed around the anus, although there was no history of rectal trouble.

Dr. Finnerud said that he could not account for a good many of the symptoms. He thought tuberculosis and syphilis had been pretty well ruled out by blood examinations and cutaneous tests, but he had not thought of thrush. Because the skin was so dry and there was a history of previous lesions about the elbows and knees, and because when the child was first seen there was an infiltrated plaque on one knee, his first impression was that it was some unusual type of ichthyosis. The skin was carefully examined generally, and no keratosis of the hair follicles was noticed at the first examination, but at the second examination, he observed patches of keratosis of the follicles on the front of each shoulder, on the extremities and in various other areas, this condition being less evident at present. The mother stated that there had been marked involvement of the scalp originally, which subsided as the other lesions appeared, and he thought there was some evidence of the disorder being pityriasis rubra pilaris.

Dr. Oliver agreed with Dr. Foerster. He did not advance any positive diagnosis but felt sure, despite the chronicity of the lesions on the palms and soles, that the disorder was acrodynia. He thought the severity and consistence of the lesions could be explained on the ground that the child had been much neglected all of its life. He had always been dirty and poorly cared for, and Dr. Oliver thought this would account for the severity of the symptoms and the ichthyotic condition of the skin. No matter what position the child was placed in, he presented the picture of abject misery, crying and whining constantly, as do patients with acrodynia. This child had not pulled out its hair or lost its teeth as yet. Dr. Oliver believed that chronic cases of acrodynia might be found as the disease is better understood. There were distinct swelling and clubbing of all the fingers, showing that more than a cutaneous condition was present.

Dr. Zwick asked whether the child perspired.

Dr. Oliver said very little, so far as he knew.

A Case for Diagnosis. Presented by Dr. Senear.

A colored man, aged 26 years, gave a history of being well until May, 1924, at which time he was vaccinated at some workman's camp. Immediately afterward, he became sick, but he was not sent into town, and soon became too ill to be moved. The body and arms were greatly swollen. He improved slightly, and started to walk away from the camp, was picked up and taken to the Cook County Hospital. There one finger was amputated, and immediately afterward the other fingers became involved in a necrotic and gangrenous process. Roentgenologic examination showed atrophic bone changes in the wrist and distal phalanges of the left hand, with a sabre-like appearance. When the hand was held down, there was less pain than when it was held up.

The Wassermann reaction was negative. This patient was demonstrated by Dr. Howard Fox at a clinic at a meeting of the American Medical Association. At that time, he had an affection of the side of the face and neck, but the hands were not nearly so much involved as at present.

DISCUSSION

Dr. Foerster said that one should consider the condition in relation to some vascular disturbance and as possibly related to Raynaud's disease or erythromelalgia, although the patient was rather young for the latter condition.

Dr. Wile said that he agreed with Dr. Foerster and thought the case might be classed in the group of Raynaud's syndrome of symmetrical gangrene. There was marked diminution of the radial pulse on one side. The history of pain fitted very well with the diagnosis of Raynaud's disease, but it was impossible to differentiate the most important feature of alternating cyanosis and blanching because the patient was a negro.

Dr. Zwick asked whether it were possible to revaccinate the patient with attenuated virus, in the hope of inciting or stimulating biologically the production of specific antibodies. Although perhaps not without some risk, he considered such a therapeutic attempt justified in view of the deplorable condition of the patient.

Dr. Senear said that they were agreed when they saw the patient at the hospital two days before that there was unquestionably some vascular change at the bottom of the condition. The acute process, the necrosis of the fingers, following so closely on an injury to the other finger made them hesitate to classify it as true Raynaud's disease, but he agreed with Dr. Wile that it was plausible to place it somewhere in that group. Replying to a question, Dr. Senear said that he did not see any suggestion of scleroderma or sclerodactylia in the case.

Lesion of Hand. Presented by Dr. Senear.

The patient was a shop foreman, aged *32*, who presented a lesion on the flexor surface of the left wrist. About ten months before presentation, he developed several reddish-brown lesions on the left palm; and about four months ago, he developed a lesion on the wrist, which appeared "like a boil." Shortly after this, he noticed a pea-sized subcutaneous nodule just above the second lesion. The second lesion was the only one which was painful. The patient had complained of stiffness of the right knee for two weeks.

Examination showed a group of papules, with some scaling, on the palm of the left hand. On the flexor surface of the wrist was a vegetating lesion about the size of a walnut, with several sinuses from which pus could be expressed. Just above this lesion was a firm, pea-sized subcutaneous nodule with no changes in the overlying skin.

DISCUSSION

Dr. Wile said that the condition looked to him like a cold abscess (tuberculous).

Dr. Harry R. Foerster agreed that it resembled a tuberculous lesion rather than a mycotic granuloma.

Dr. Foerster said he thought the association with the ganglion of the tendon sheath would carry some weight in favor of the tuberculous nature of the condition.

Dr. Finnerud said he thought the question could be settled by means of a biopsy.

Dr. Senear said that he had thought of the possibility of tuberculosis and of some mycotic process, blastomycosis or sporotrichosis, but the lesions on the palms were distinct papules with sharply demarcated scales, and this did not seem to be in keeping with any of these diagnoses. Because of the history that the lesion on the wrist began as a boil-like condition, he had thought of the possibility of this being a secondary process, with a simple granulomatous lesion developing.

[Note.]—The lesion on the wrist was excised, and microscopic examination showed simple granulation tissue.

A Case for Diagnosis. Presented by Drs. Pusey and Senear.

A woman, aged 40, six years before presentation had an eruption which appeared on the outer areas of both great toes. New lesions had gradually appeared, two on the right calf and one, the latest, had appeared two years before on the right forearm. The lesions had gradually enlarged in spite of treatment, although there had never been any ulceration.

There was no history of previous illness or any form of tuberculosis in the patient or her family. The Wassermann reaction one year before was negative, and she had not improved under antisyphilitic therapy. She had used various ointments locally and pills internally, and had received "electrical treatments" elsewhere.

A biopsy showed hyperkeratosis with thinning of the rete pegs and necrosis in the corium. Deep in the corium and subcutaneous tissue there was perivascular, round cell infiltration and slight endothelial proliferation. There were no plasma and no giant cells.

DISCUSSION

Dr. Foerster said he thought that lupus erythematosus, granuloma annulare and scleroderma were the three conditions to be considered. In the brief time they had to examine the case and in the absence of a biopsy, he thought that circumscribed scleroderma would be the most probable diagnosis. The plate-like infiltration was such as is found in circumscribed scleroderma, and the presence of several tiny, marginal occlusion cysts would not invalidate that diagnosis.

Dr. Stillians said he thought it was an atypical granuloma annulare, judging both from the clinical appearance and the report on the biopsy.

Dr. Mitchell said that he had thought of granuloma annulare. The case greatly resembled one which they studied some years ago in which there were discrete lesions up the arms, which healed in the center, with a rolled hard border. Similar lesions were present in this case, and when traction was put on the border it assumed a yellowish appearance, which also was characteristic of the case they studied over several years. The lesions on the arms particularly resembled the case they had studied histologically.

Dr. Lieberthal said that this was demonstrated by him with histologic slides at the February, 1924, meeting of the Society as one of scleroderma, to which diagnosis he still adhered on the strength of the clinical and especially the histologic findings. The patient had then been receiving thyroid substance and diathermic applications over a period of several months, without any benefit.

Dr. Senear said that they had considered the various points which Dr. Foerster had mentioned but had not yet arrived at a definite diagnosis.

Dermatitis Herpetiformis. Presented by Drs. Oliver and Finnerud.

A girl, aged 1 year and 10 months, was in good health, and there was no history of any skin disease in the other three children in the family. When the patient was first seen one month previously, she had a generalized itching eruption of several days' duration, and there was a history of a similar attack two months previously. The mother stated that the lesions began as water blisters, which were either scratched open or which she was able to clear up with a zinc oxid ointment.

At the time of the first examination, the patient showed numerous pea-sized and larger erythematous macules and papules, most of them on the buttocks, and an occasional lesion on the extensor surface of the arms. Numerous hyperpigmentations were present as relics of the previous attack, which apparently had involved the buttocks and shoulders.

DISCUSSION

Dr. Lieberthal said that he accepted the diagnosis.

Dr. Mitchell said that the bright red appearance of the papules suggested the lesions frequently seen on the buttocks in children as the result of follicular infection, and in the absence of an eosinophilia he thought one would hesitate as to the diagnosis of dermatitis herpetiformis.

Dr. Wile called attention to the group of pigmented lesions between the shoulders, which were obviously the result of a previous attack. They were definite pigmented macules and distinctly grouped.

Dr. Finnerud said that the only other pigmented spots that remained from the previous attack were on the extensor surfaces of the arms and forearms.

Dr. Oliver said that he had not had much opportunity to study this patient, but in two other cases which he had reported previously he had kept careful notes and was comparing the three cases. All the patients were placed on arsenical therapy, and all had recovered. He thought the disorder was dermatitis herpetiformis, but he believed these cases in children were amenable to treatment. The lesions had consisted of vesicles, papules and bullae.

Psoriasis. Presented by Dr. Waugh.

A boy, aged 11 years, presented a disorder of three years' duration. The lesions were practically limited to the hands and feet, and consisted of large, erythematous, exfoliated patches, shiny in appearance, with the margins sharply defined. They were always dry and accompanied by some itching, and were present principally on the palmar and plantar surfaces.

DISCUSSION

Dr. Lieberthal said that he thought it was an interesting case of psoriasis because of the localization of the lesions.

Dr. O'Leary said that he was not satisfied in his own mind that the patient had psoriasis. The condition looked definitely mycotic, he thought, and if this process was psoriatic, the boy would have shown definite psoriasis of the nails or scalp in addition. He felt the grouped follicular lesion of the sternum was not psoriatic.

Dr. McEwen said that he was doubtful as to the diagnosis of psoriasis, considering the history of the case and the persistent localization of the lesions on the hands and feet.

Dr. Foerster said he thought that one should consider epidermolysis bullosa in this connection, but he had no diagnosis to offer.

Dr. Wile agreed with Dr. O'Leary. He could not see that the diagnosis of psoriasis was justified, particularly in view of the character of the eruption on the chest, which was made up of a group of distinct follicular hyperkeratotic plugs.

Dr. Pusey said that Dr. O'Leary had expressed his idea very well. He had thought of various things that occurred on the palms, but he was not satisfied with the diagnosis of psoriasis, and he did not think the satellite lesion on the body bore this out.

Dr. Zwick said he thought, at least from the clinical picture as it presented itself, that one should take into consideration, or investigate by laboratory methods (Sabouraud's or more conveniently Lewandowsky's culture method), such conditions as epidermolysis bullosa acquisita (Wise), Audry's phlyctenosis bullosa, streptoderma bullosa pedum et manuum.

Dr. Finnerud said that he had thought only of psoriasis. He had seen psoriasis limited to the palms and soles and also in association with body lesions, which presented the same type of lesions as in this case.

Dr. Senear was not convinced of the correctness of the diagnosis, and he thought that an abortive form of pityriasis rubra pilaris should be considered. The follicular, horny papules on the chest and the symmetrical scaling eruption on the palms and soles suggested this diagnosis. He did not see the bullous lesions which others had described, but in spite of this thought Devergie's disease was a possibility.

Dr. Mitchell said that he did not think there was much suggestion of psoriasis in the condition of the palms at present. It was a smooth, shiny process, with no suggestion of psoriasis elsewhere. He thought the bullous lesions on the feet and the grouped follicular keratoses on the sternum should be considered in arriving at a diagnosis.

Dr. Pusey said that the chronic inflammatory process of the hands known as dermatitis repens should be mentioned.

Dr. Mitchell said that the case lacked the undermining pustular process seen in dermatitis repens.

Dr. Oliver said that he thought the case resembled one shown by Dr. Hedge which had been treated by the roentgen ray. In that case the condition was perhaps more scaly, but it was shiny like the present one.

Bromid Eruption. Presented by Dr. Waugh.

A woman, aged 28 years, began taking Bromo Seltzer for the relief of headaches six months before presentation. The dosage was gradually increased, until she took from one to two teaspoonfuls four times daily. When she was first seen, two months before presentation, she had a papulopustular rash over the shoulders, back and lower extremities. The lesions were bluish red, and some of those on the legs were crusted. There was no history of a skin eruption until she began taking Bromo Seltzer. During the past two months, the lesions on the body had largely disappeared. Some of those on the lower extremities had developed into ulcers, resembling somewhat erythema induratum, but no history of deep-seated nodules preceding the ulcers could be secured.

DISCUSSION

Dr. Wile said that he could not consider the case a bromoderma, but he thought it a typical case of erythema induratum, associated with papulonecrotic lesions, presumably of tuberculous nature, on the forearm and legs. In his opinion, the fact that the patient had taken Bromo Seltzer was only a misleading factor in the history. There were no lesions which suggested bromoderma so far as he could see.

Dr. Senear said that Dr. Waugh had been obliged to leave early, but that he had requested him to say that until recently there had been no induration in the lesions and no ulceration; he had thought of the possibility of erythema induratum and papulonecrotic tuberculid, but could not entertain these as the diagnosis because of the appearance of the lesions.

Dr. Senear said he thought it was a case of erythema induratum.

Dr. Mitchell said he thought the lesions around the elbows were probably tuberculids, and the punched-out appearance of the ulcers at the shoe tops led him to conclude that the diagnosis was erythema induratum.

Two Cases of Leprosy. Presented by Drs. Stillians and Oliver.

Case 1.—A woman, aged 35, a native of Trinidad, had a disorder which was of six years' duration and of the macular anesthetic type. Her eyebrows had entirely fallen out, and she had a macular eruption on the forearms. Bacilli had been found in the nasal secretion. Since entering the hospital a few months before and beginning treatment with chaulmoogra oil, she had shown improvement.

Case 2.—A woman, aged 23, a native of Mexico, had a disorder which began four months previously with pain in the right knee, wrist and ankle. She presented a typical maculopapular eruption on the back and arm. Bacilli had been found in the nasal secretion.

DISCUSSION

Dr. Zwick asked what was being done in the way of treatment with Hoffmann's or Dean's chemical derivatives of chaulmogra oil.

Dr. Oliver said that the first patient came into town during the summer and was now receiving as much chaulmoogra oil as she could tolerate. She had a brother in the South who was a physician, and who had treated her for a number of years for an unusual case of pellagra. Organisms had been demonstrated in smears from the nose.

The other patient was receiving the same therapy. They hoped to get these two patients and one other into the government leprosarium some time in the fall.

Lupus Vulgaris of Glans Penis. Presented by Drs. Stillians and Oliver.

A colored man, aged 42, presented a lesion on the head of the penis. This had been present one year, appearing as a small pimple, and gradually ulcerating and enlarging. The ulcer occupied the whole lower surface of the glans, was of jagged outline and irregular base and resistant to all local medication. A section showed typical tubercle formation with giant cells.

DISCUSSION

Dr. Oliver said that sections had been taken and the diagnosis of tuberculosis verrucosis cutis confirmed. The patient was an intelligent negro and was anxious to know what treatment should be carried out, particularly as to whether amputation should be performed.

Dr. Mitchell said that an old Greek had been coming to the Central Free Dispensary for some time, who had a lesion on the penis which resembled this one very much except that it was considerably larger. He refused to submit to a biopsy. The Wassermann reaction was positive, but he had

received intensive arsphenamin therapy with no effect on the lesion. It apparently was not carcinomatous, but it refused to heal.

Dr. Pusey said that he would not advise amputation, for surgery is not very successful in tuberculous lesions. He would give the patient as good care as possible, and if any therapy was used would advise the ultraviolet light.

Dr. Wile said that lesions of this kind and in this location if untreated were likely to undergo malignant degeneration. If the lesions involved only the glans, if it were a local process, he thought it might be well to amputate, in view of the danger of carcinomatous degeneration.

Dr. Zwick said that in similar cases with tuberculous lesions he obtained good results by the application of pyrogallic acid in ointment or Beck's paste form. The applications are made daily in weekly cycles or series of alternating strong (5 to 20 per cent.) and weak (0.5 to 1 per cent.) concentrations. Pyrogallic acid has a selective action on the tuberculous tissue (Veiel), but its use is accompanied by considerable pain. To combat this, anesthesin or cycloform is first dusted on the ulcer and then it is immediately covered with the paste, as exposure to air causes excruciating pain. If after from five to ten days the ulcer appears clean, it is allowed to heal under the weaker applications. The cycles have to be repeated several times. If the pain is unbearable, general analgesics may have to be administered.

Dr. O'Leary called attention to the fact that tuberculosis of the glans penis is frequently the result of extension from a tuberculous process higher up in the genito-urinary tract. The few cases of tuberculosis of the penis that have been seen in the Mayo Clinic have all been associated with a kidney or bladder tuberculosis.

Blastomycosis of the Nose. Presented by Drs. Stillians and Oliver.

A negro, aged 40, presented two large verrucous lesions on the nose, one in the lobe of the ear and another on the third finger of the left hand. These had been present only a few months, those on the nose having appeared since his admission to the hospital for genito-urinary disease two weeks previous to the meeting. On the right ala nasi was a mushroom-like growth 2 cm. in diameter. The other lesions were smaller and flatter, some of them verrucous. A section of one of these showed marked acanthosis, and epidermal abscesses containing blastomyces.

PITTSBURGH DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Oct. 16, 1924

H. G. Wertheimer, M.D., *Presiding*

Recklinghausen's Disease. Presented by Dr. Phillips.

L. B., a man, aged 42, a janitor, presented hundreds of lesions varying in size from that of a pea to that of a goose egg. These tumors were distributed over the scalp, face, eyelids, neck, trunk and extremities. The skin over them was normal in some places, atrophic in others and hypertrophic in a few places. The color varied from normal skin color to a violaceous hue. The skin over various parts of the body showed many macular pigmented areas of varying size. The patient never progressed beyond the second grade

in school, nor did his sister and two brothers who were similarly affected. None of his ancestors so far as could be ascertained had any such skin trouble, nor do the children of his sister or brother.

DISCUSSION

DR. CRAWFORD said that cases of this type are interesting from a dermatologic point of view, but that they should be seen in conjunction with a neurologist, as they show many conditions affecting the nervous system, especially such as are due to pressure on the spinal cord.

DR. PHILLIPS said he thought that the point made by Dr. Crawford was valuable, and symptoms referable to the nervous system could be elicited in the patient presented. He walked with difficulty and tired easily. He said he would have a neurologist examine the patient.

SCLERODERMA. Presented by DR. HOLLANDER.

A woman, aged 32, American, a housewife, presented a linear band of six months' duration, about 3½ inches (9.5 cm.) long, extending from behind the right ear downward along the sternomastoid. The skin was inelastic, firm and smooth; the central part was white; the borders were pigmented. There was a noticeable improvement of the lower part of the lesion from unfiltered doses of ¼ roentgen-ray unit weekly.

DISCUSSION

DR. BARR said that he was very much interested in the case on account of the progress made under roentgen-ray treatment.

CARCINOMA (PRICKLE-CELL TYPE). Presented by DR. WERTHEIMER.

A man, aged 63, presented at the inner canthus of the left eye a cherry sized, indurated cauliflower-like mass; to the right of this mass, a similar growth was present, which was adherent to the ocular and bulbar conjunctivae. Over the bridge of the nose was a walnut sized, flat tumor, fluctuating in the center, the edges of which undermined the periosteum. There was a complete blocking of the left nares with a mass, grayish-white in appearance, slightly glandular, with well developed blood vessels coursing over it; it was firm on palpation, and the area of attachment could not be ascertained, although the margin was free as far back as could be palpated. The tumor at the inner canthus began ten years before presentation, at the site of a vascular nevus, and grew gradually. Two years later, the patient was treated with radium, which caused almost complete disappearance of the lesion. Three years ago, it again began to enlarge, and a second lesion appeared. Over the bridge of the nose, the mass had been present about two months. There was never any pain. The Wassermann test was negative.

DISCUSSION

DR. GUY said that the condition was of course some form of malignant growth, but that one could not definitely state the type.

DR. PHILLIPS asked to have a biopsy, which he said could be obtained without any danger with electrocautery or desiccation.

A CASE FOR DIAGNOSIS. Presented by DRS. SCHWARTZ and BUSMAN.

A woman, aged 31, a housewife, presented a fungating tumor mass of the left ala nasi and cheek about the size of a hickory nut. A similar lesion of

larger size involved the portion of the face around the left angle of the mouth. Two split pea sized lesions were present below the right angle of the mouth. The individual growths were rather soft and painless, and showed numerous distended capillaries. They bled freely on puncturing, but there was no ulceration. The lesions first appeared five months before presentation, beginning as small papules. At times they gave off a serous discharge when irrigated by local application.

DISCUSSION

Dr. Beinhauer suggested several possibilities: a toxic eruption such as erythema multiforme, or a drug eruption, as from bromides, or a bullous lupus erythematosus, or one due to a fungus. He noticed typical dried bullae about and on the lesions. The lesions were soft.

Dr. Guy said that the lesions were due either to a drug, such as bromids or iodids or a rapidly growing tuberculous condition, but he leaned towards the diagnosis of drug eruption.

Dr. Phillips said that in the absence of any drug eruption he would favor the diagnosis of tuberculosis. He had seen a similar case at New York Academy, where biopsy proved the diagnosis.

Dr. Crawford said that he thought the condition was a bromid eruption. He certainly could not consider the diagnosis of tuberculosis, especially since one lesion disappeared without leaving the slightest sign.

Dr. Hollander called attention to a case of tuberculosis of the skin about the mouth and affecting the mucous membrane, which was presented before the society within the last year. The case presented a similar eruption — soft, elevated, painless and a much brighter red than one ordinarily associates with tuberculosis. The case quoted proved to be tuberculosis. That patient showed healed lesions where one could hardly discern any scar or pigmentation. Dr. Hollander favored the diagnosis of tuberculosis.

Dr. Wertheimer said he thought the condition was a drug eruption caused by bromid or iodid. He said that on account of its color he could not accept the diagnosis of tuberculosis or lupus tumidus.

Lester Hollander, M.D. Secretary.

Book Review

PATHOGENIC MICROORGANISMS. PARK and WILLIAMS, Eighth edition, 211 engravings and 9 full page plates. Price $6.50. Philadelphia: Lea & Febiger.

The fact that this is the eighth edition of this work on bacteriology is sufficient evidence of the esteem in which it is held. As originally published, it was based on the practical experience of the bacteriologic laboratories of the city of New York, and doubtless the practical emphasis which this basis of production gave it is largely responsible for its popularity. It covers not only bacteriology, but all forms of pathogenic micro-organisms. It is a highly useful book.

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